6277969

APPROVED O.G. FIG.
BY CLASS SUBCLASS
DRAFTSMAN

8621806 1986-12-16

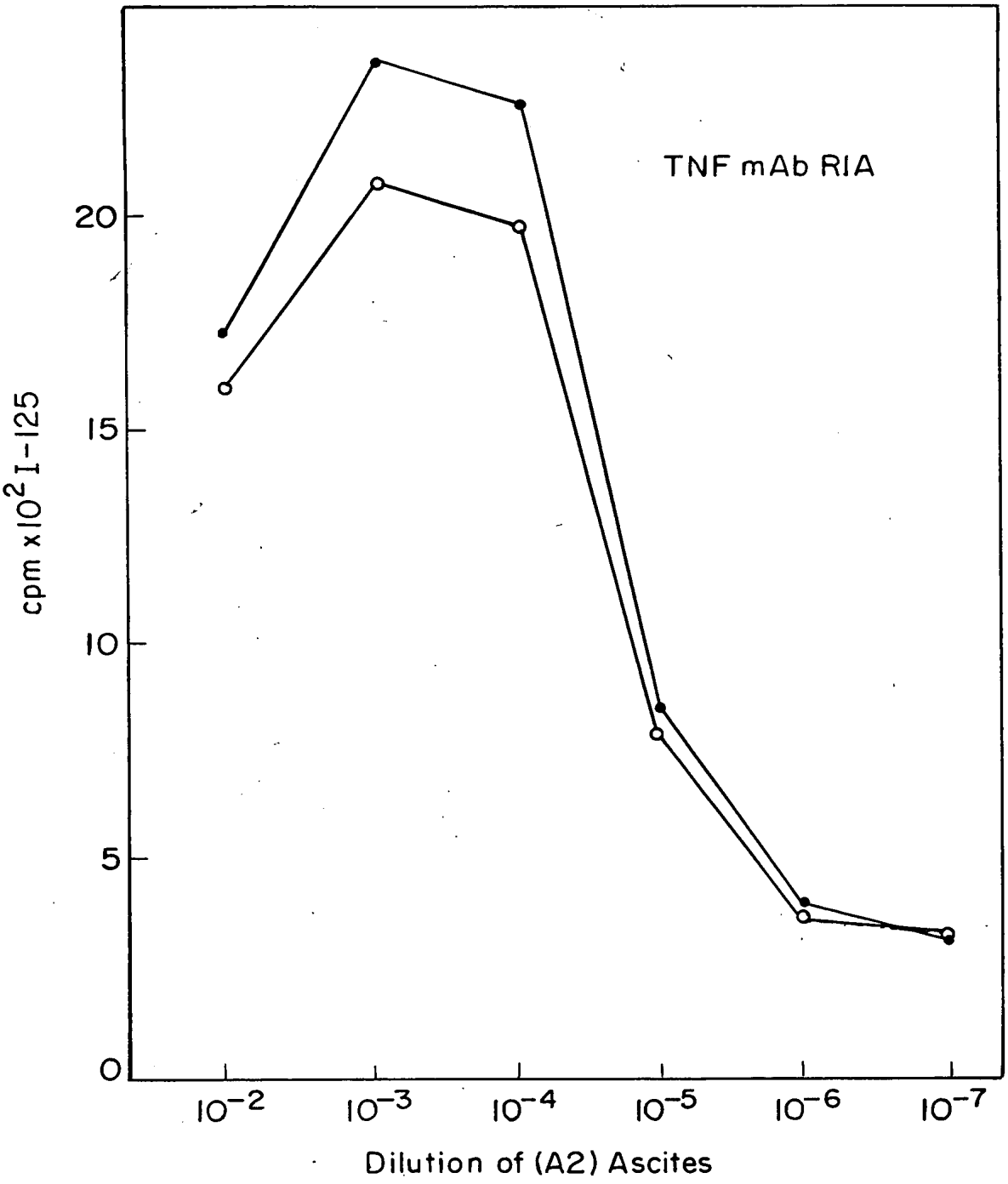


FIG. 1

O.G. FIG.
APPROVED
CLASS. SUBCLASS
BY
DRAFTSMAN

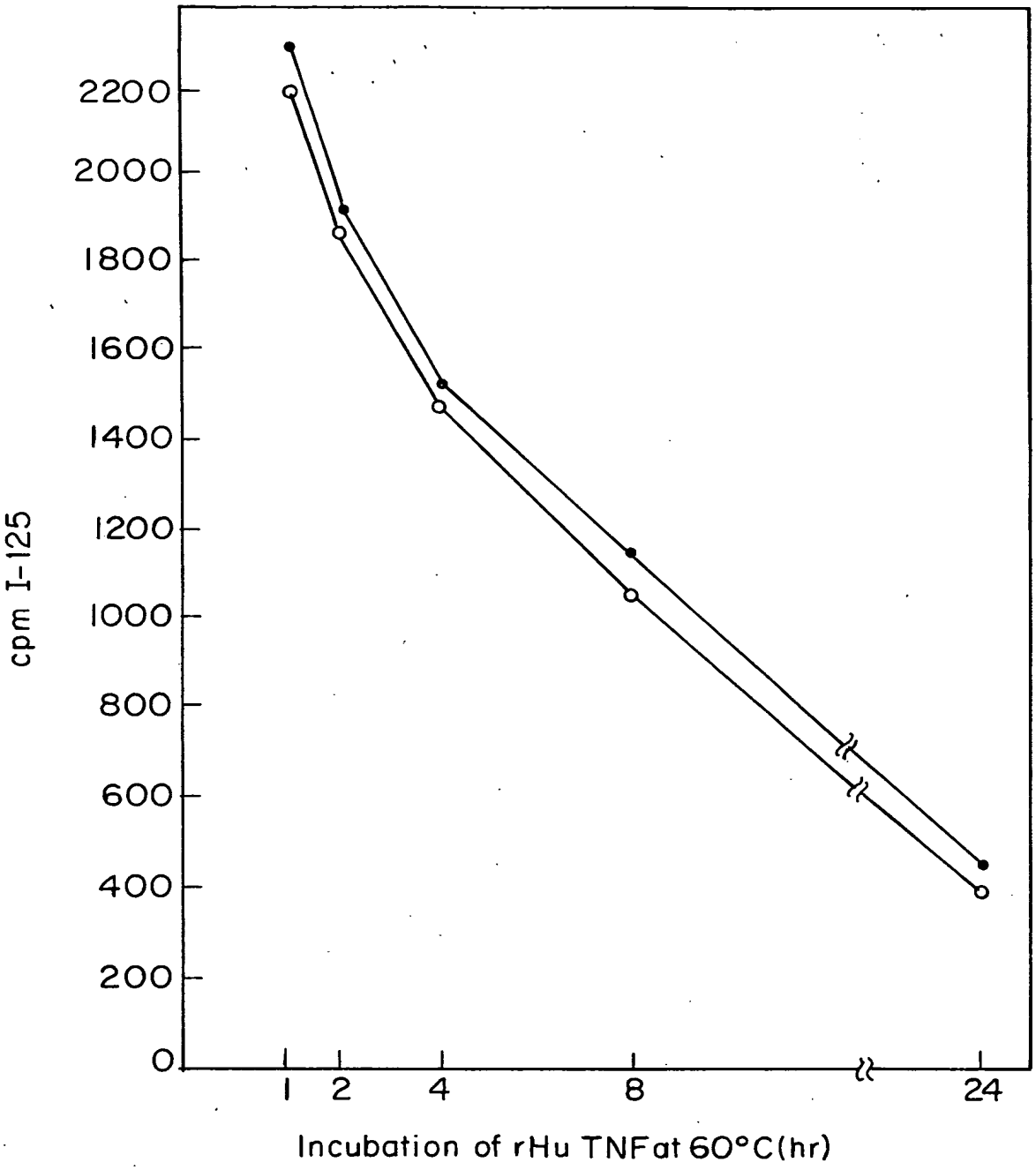


FIG. 2

APPROVED BY DRAFTSMAN
O.G. FIG.
CLASS
SUBCLASS

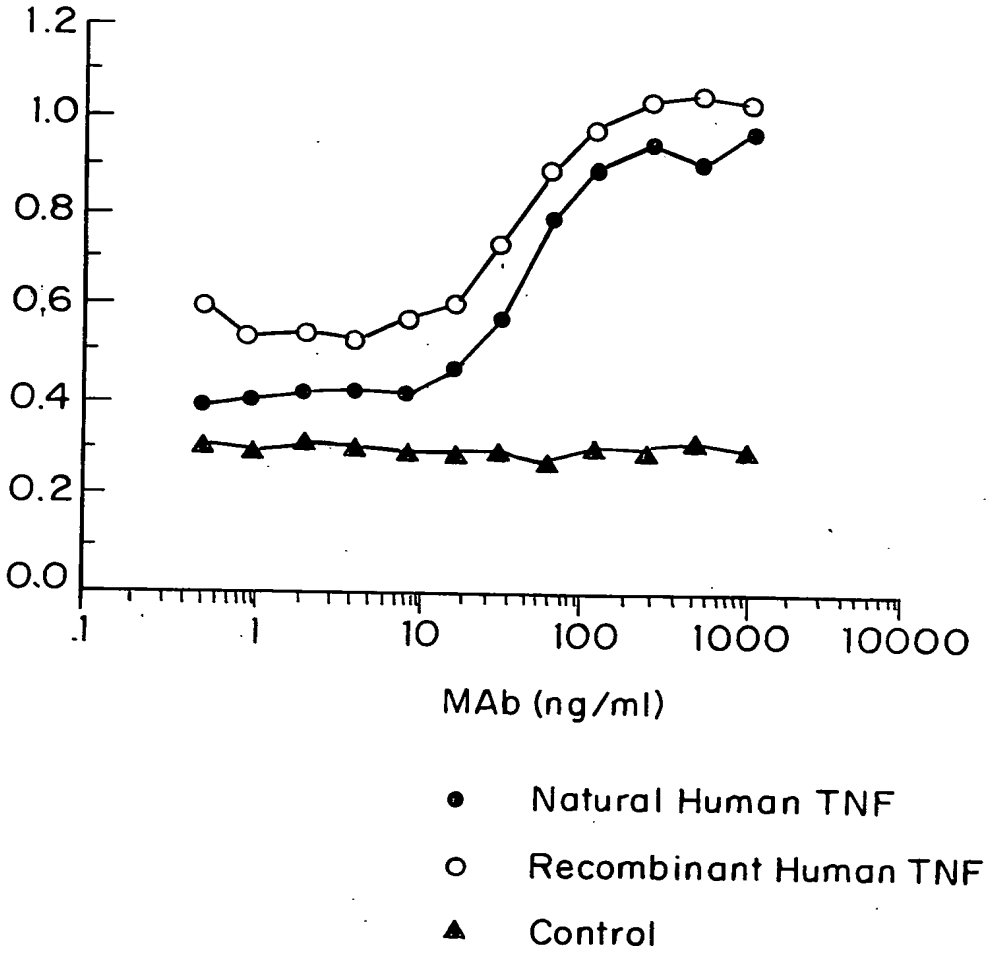


FIG. 3

862T80 "6TTEET6C
APPROVED BY DRAFTSMAN | O.G. FIG. | CLASS | SUBCLASS

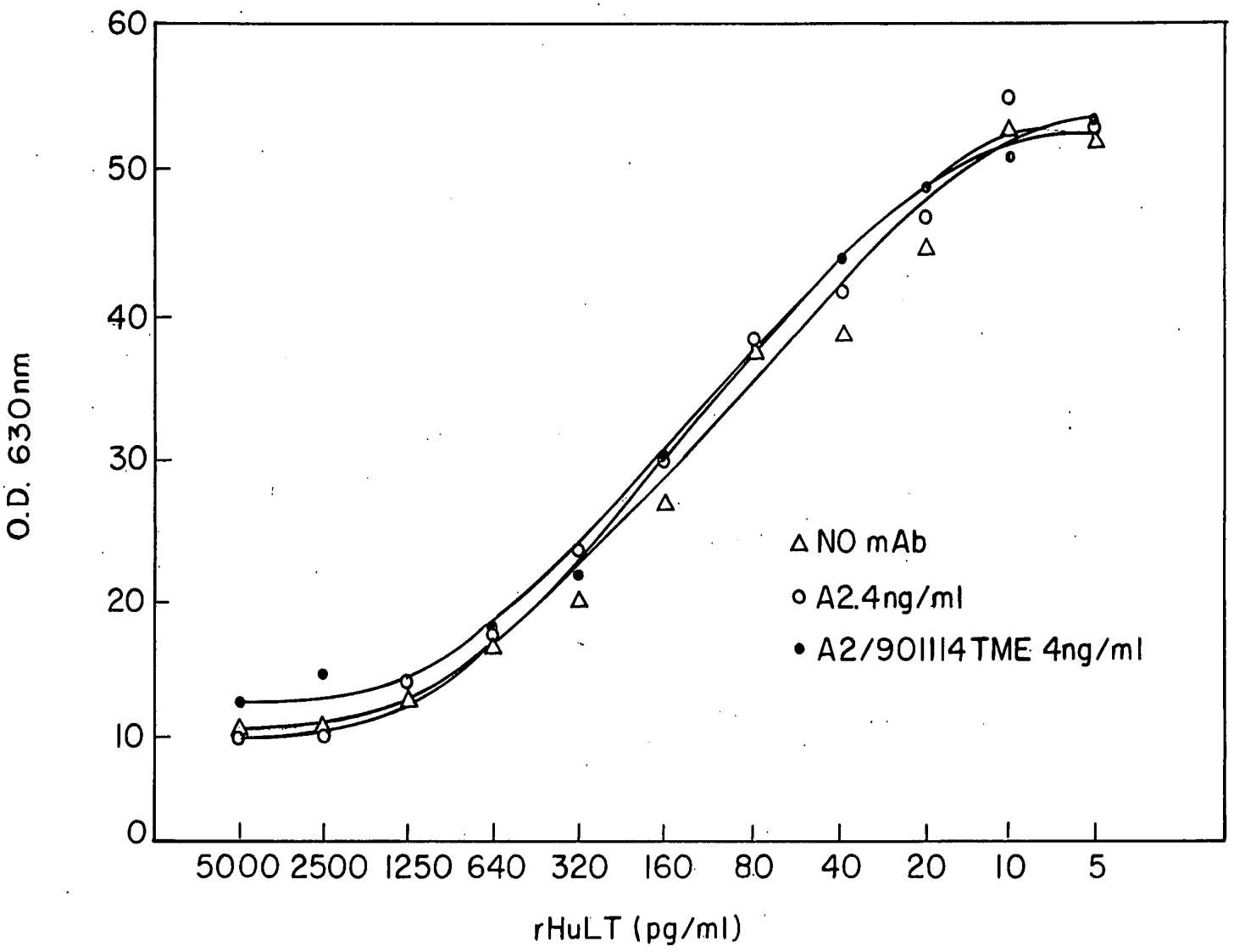


FIG. 4

862780 SHEET 5 OF 6
APPROVED BY DRAFTSMAN | O.G. FIG. | CLASS | SUBCLASS

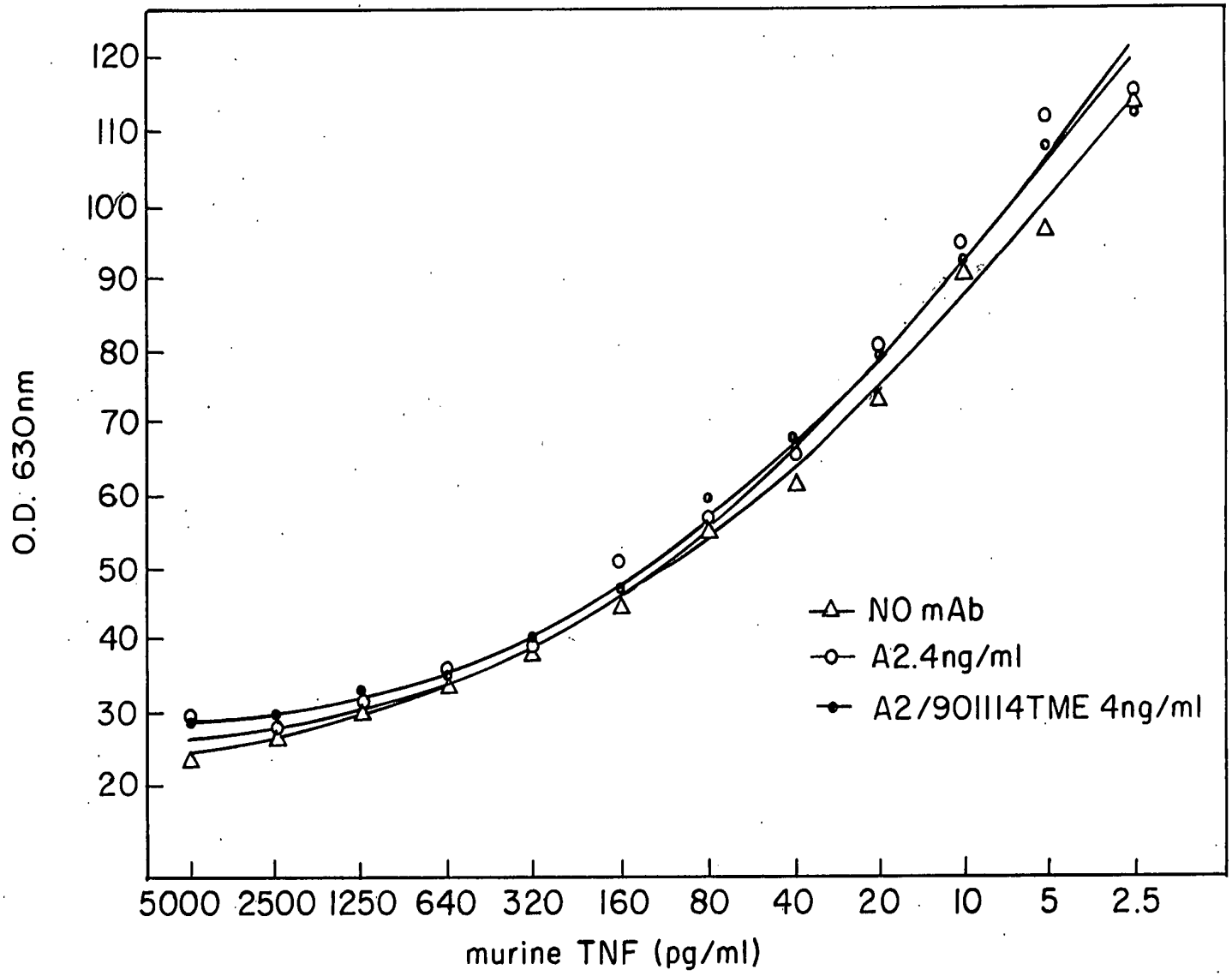


FIG. 5

862780 STREET
APPROVED BY DRAFTSMAN
O.G. FIG.
CLASS. SUBCLASS

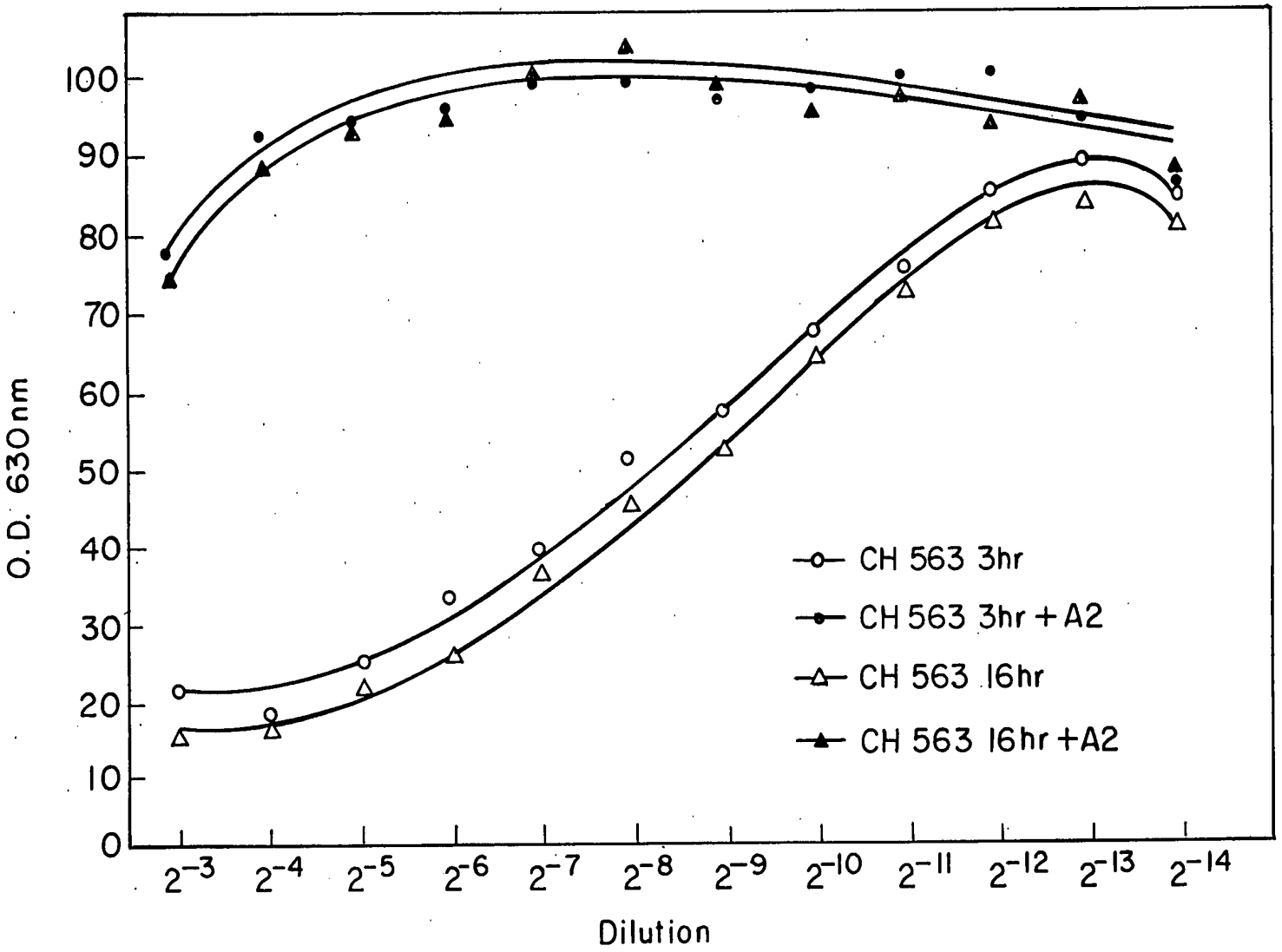


FIG. 6

862180 SHEET 60

APPROVED BY DRAFTSMAN | O.G. FIG. CLASS SUBCLASS

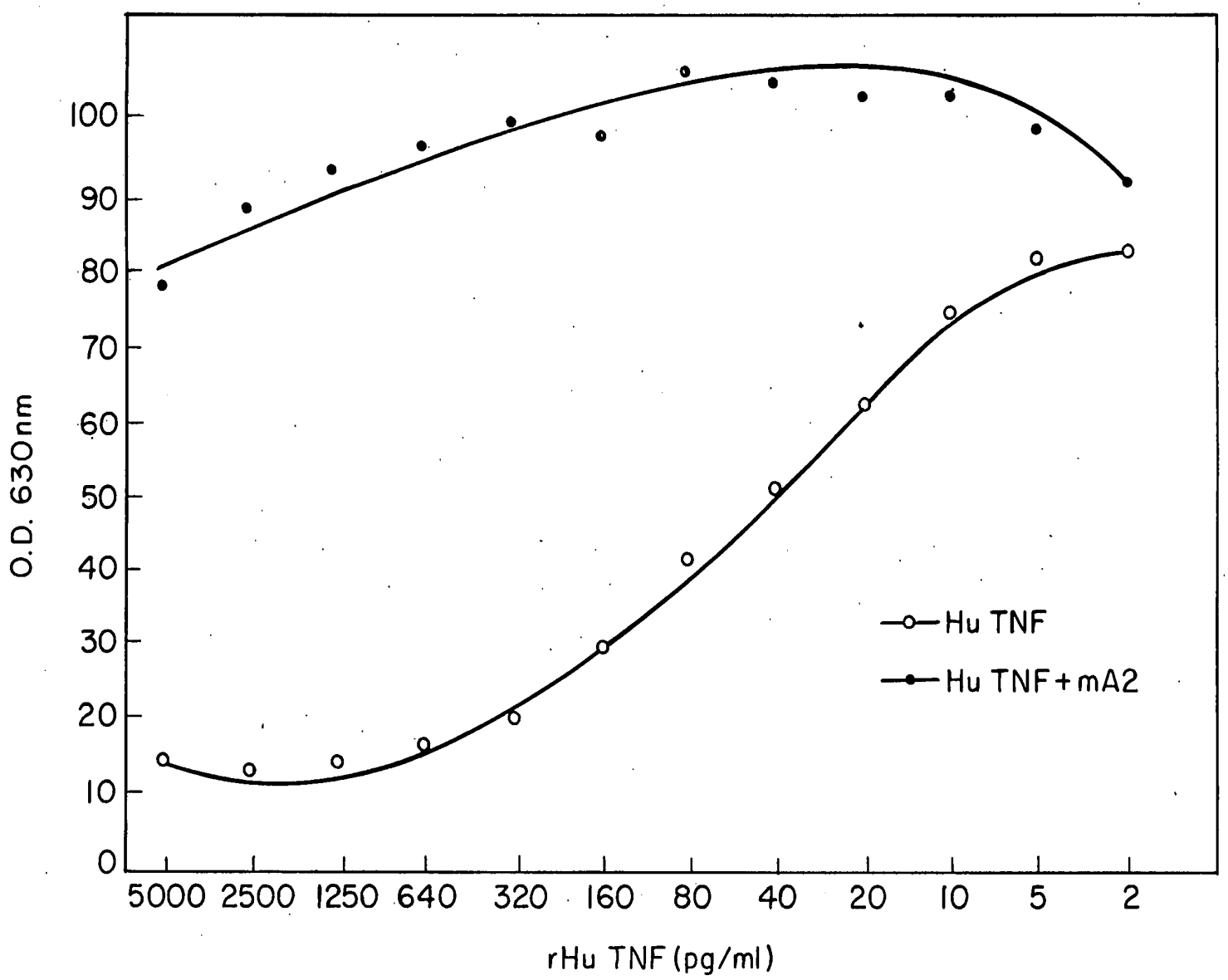
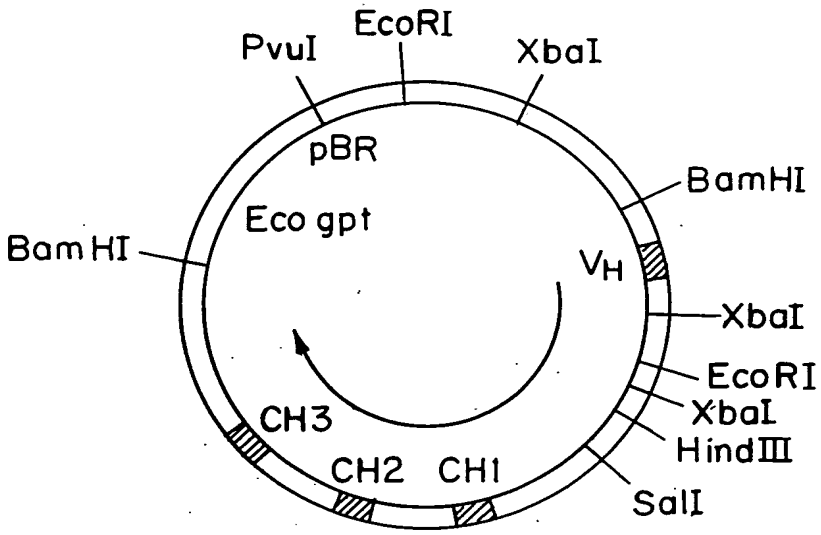


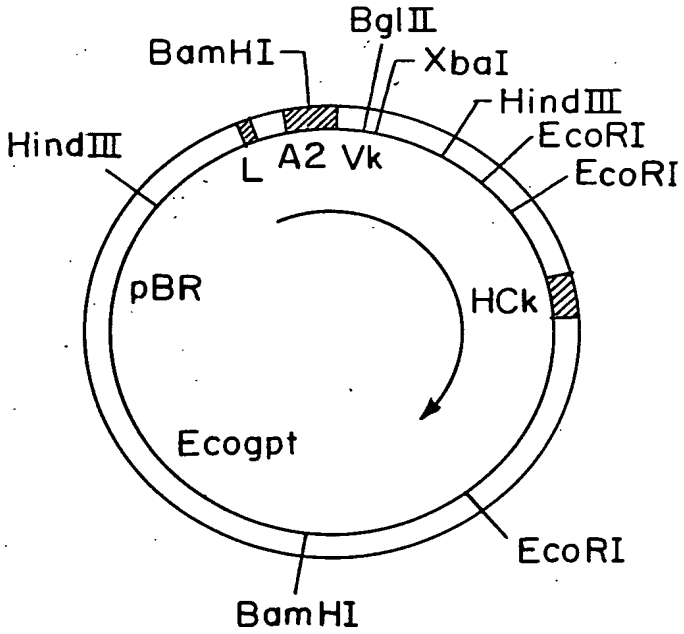
FIG. 7

APPROVED O.G. FIG.
CLASS SUBCLASS
BY
DRAFTSMAN



pA2HG1apgpt

FIG. 8A



pA2HuKapgpt

FIG. 8B

APPROVED BY DRAFTSMAN
O.G. FIG.
CLASS
SUBCLASS

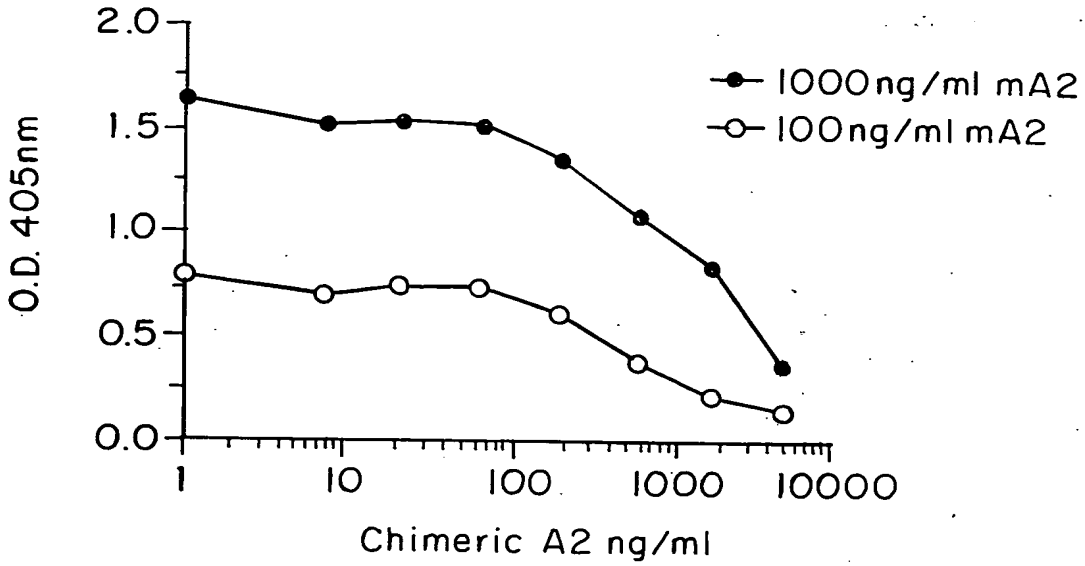


FIG. 9A

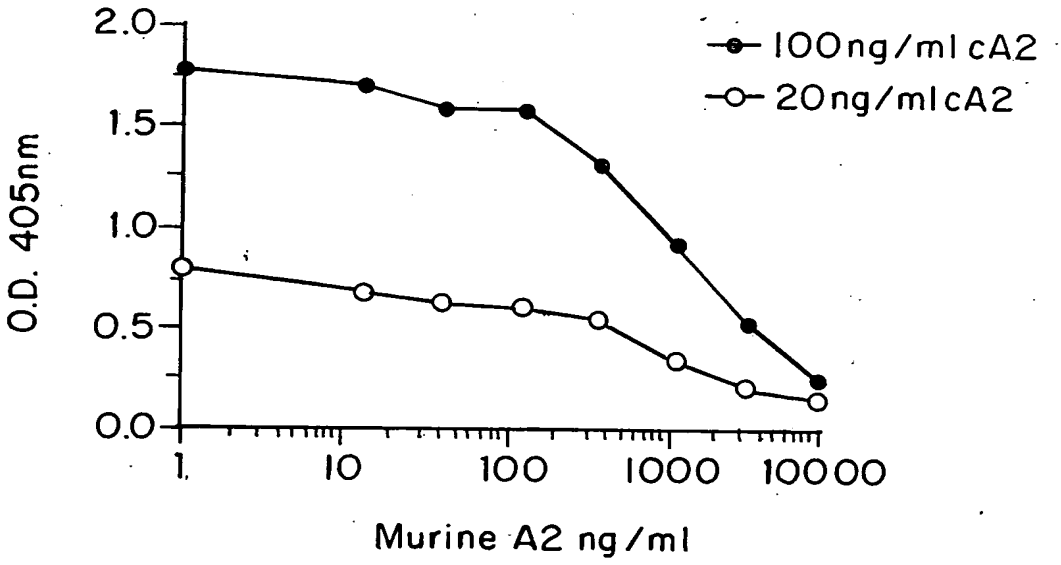


FIG. 9B

APPROVED BY DRAFTSMAN
CLASS SUBCLASS
FIG.

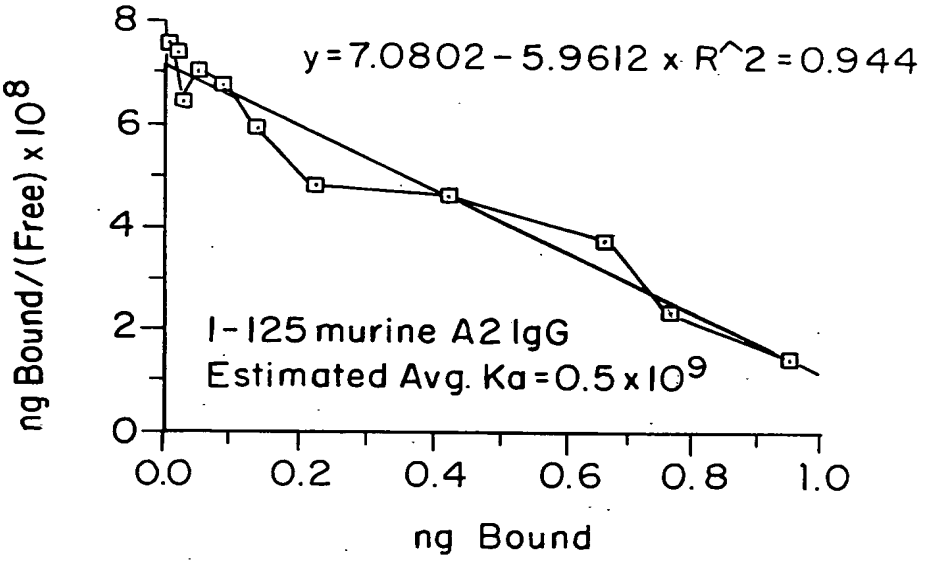


FIG. 10A

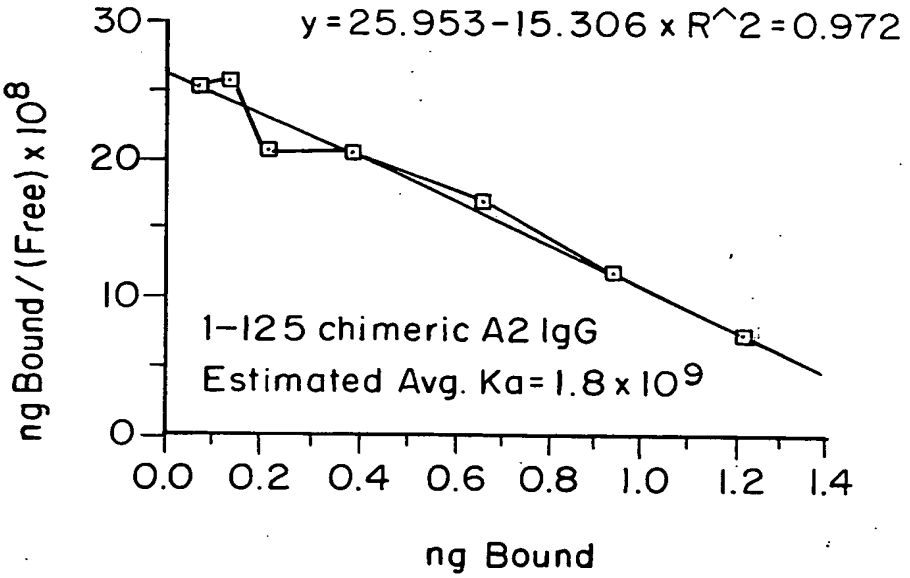


FIG. 10B

APPROVED O.G. FIG.
CLASS SUBCLASS
BY DRAFTSMAN

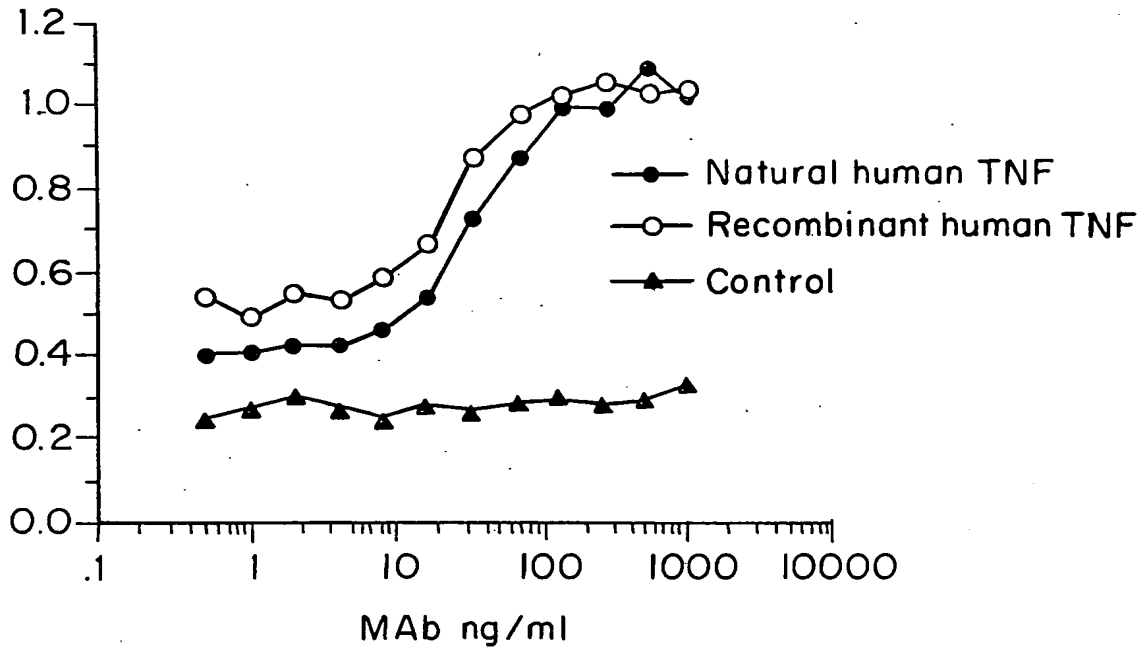


FIG. 11

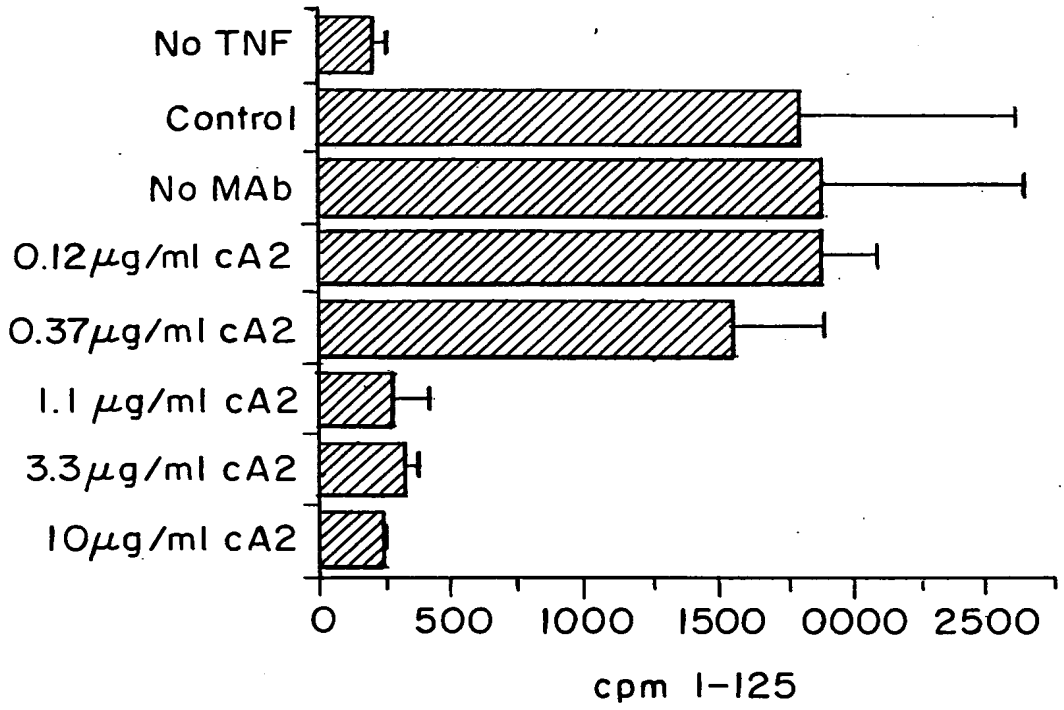


FIG. 12

862180 "6TTEET60

APPROVED BY DRAFTSMAN | O.G. FIG. CLASS | SUBCLASS

```
1                                                  10
Val Arg Ser Ser Ser Arg Thr Pro Ser Asp Lys Pro Val Ala His Val Val Ala Asn Pro

21                                                 30
Gln Ala Glu Gly Gln Leu Gln Trp Leu Asn Arg Arg Ala Asn Ala Leu Leu Ala Asn Gly

41                                                 50
Val Glu Leu Arg Asp Asn Gln Leu Val Val Pro Ser Glu Gly Leu Tyr Leu Ile Tyr Ser

61                                                 70
Gln Val Leu Phe Lys Gly Gln Gly Cys Pro Ser Thr His Val Leu Leu Thr His Thr Ile

81                                                 90
Ser Arg Ile Ala Val Ser Tyr Gln Thr Lys Val Asn Leu Leu Ser Ala Ile Lys Ser Pro

101                                               110
Cys Gln Arg Glu Thr Pro Glu Gly Ala Glu Ala Lys Pro Trp Tyr Glu Pro Ile Tyr Leu

121                                               130
Gly Gly Val Phe Gln Leu Glu Lys Gly Asp Arg Leu Ser Ala Glu Ile Asn Arg Pro Asp

141                                               150
Tyr Leu Asp Phe Ala Glu Ser Gly Gln Val Tyr Phe Gly Ile Ile Ala Leu
```

FIG. 13

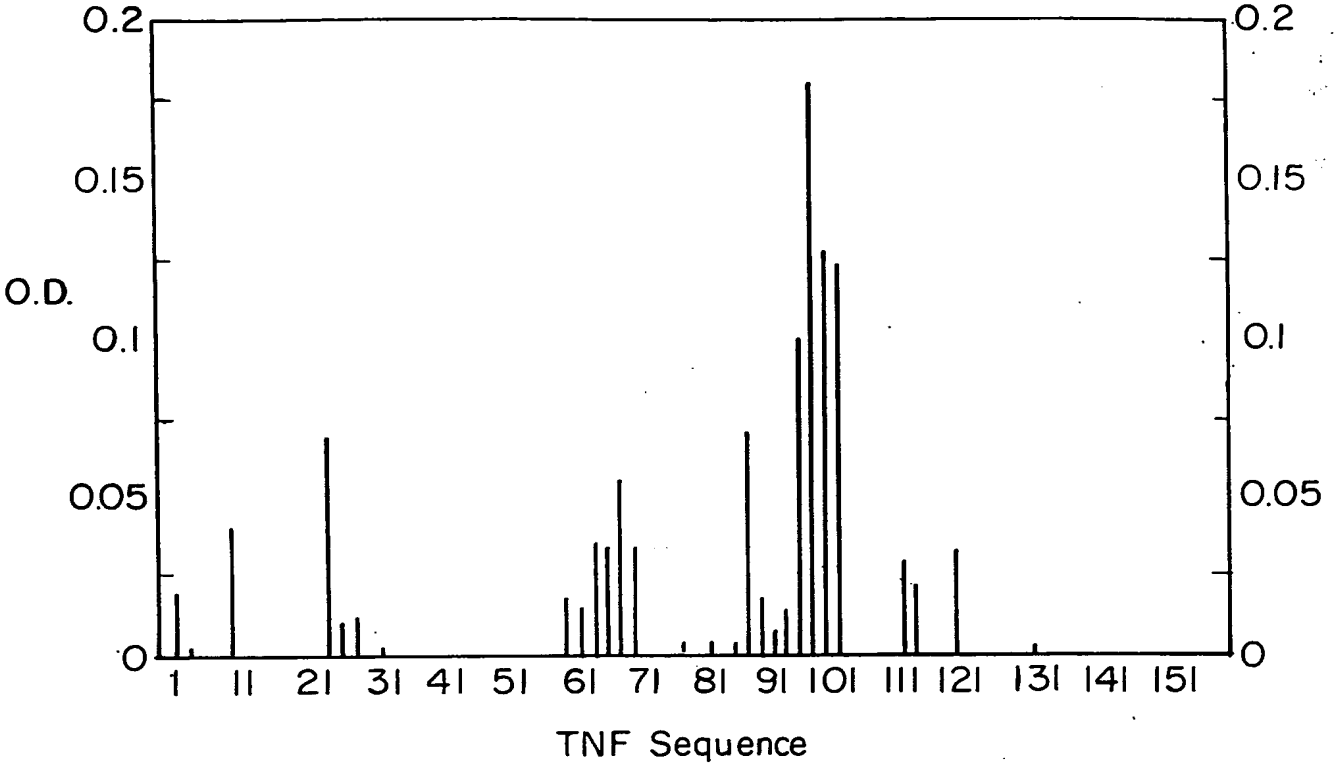


FIG. 14A

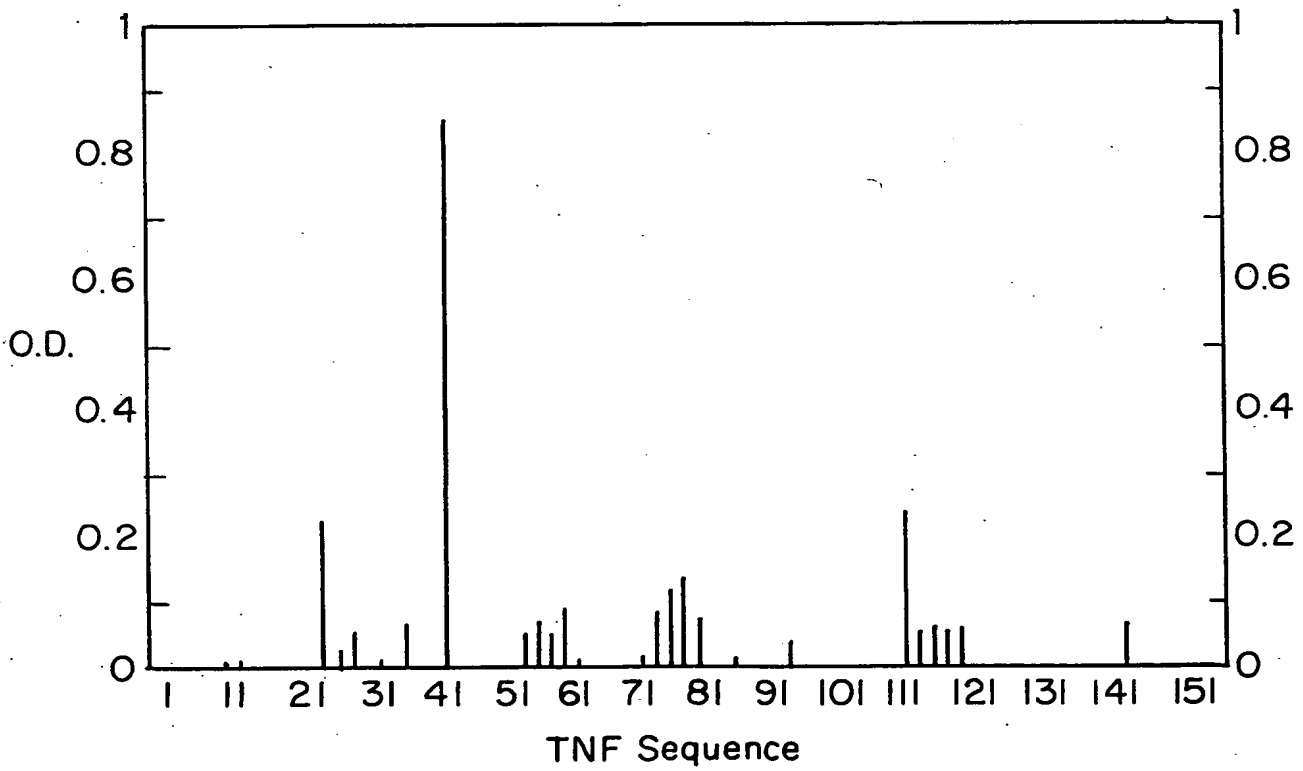


FIG. 14B

APPROVED O.G. FIG.
CLASS SUBCLASS
DRAFTSMAN
BEST AVAILABLE COPY

862T80"6TTEET60

```
1                                                  10
Val Arg Ser Ser Ser Arg Thr Pro Ser Asp Lys Pro Val Ala His Val Val Ala Asn Pro

21                                                 30
Gln Ala Glu Gly Gln Leu Gln Trp Leu Asn Arg Arg Ala Asn Ala Leu Leu Ala Asn Gly

41                                                 50
Val Glu Leu Arg Asp Asn Gln Leu Val Val Pro Ser Glu Gly Leu Tyr Leu Ile Tyr Ser

61                                                 70
Gln Val Leu Phe Lys Gly Gln Gly Cys Pro Ser Thr His Val Leu Leu Thr His Thr Ile

81                                                 90
Ser Arg Ile Ala Val Ser Tyr Gln Thr Lys Val Asn Leu Leu Ser Ala Ile Lys Ser Pro

101                                               110
Cys Gln Arg Glu Thr Pro Glu Gly Ala Glu Ala Lys Pro Trp Tyr Glu Pro Ile Tyr Leu

121                                               130
Gly Gly Val Phe Gln Leu Glu Lys Gly Asp Arg Leu Ser Ala Glu Ile Asn Arg Pro Asp

141                                               150
Tyr Leu Asp Phe Ala Glu Ser Gly Gln Val Tyr Phe Gly Ile Ile Ala Leu
```

FIG. 15

862780 6TTEET60

GACATCTTGCTGACTCAGTCTCCAGCCATCCTGTCTGTGAGTCCAGGAGAAAGAGTCAGT
AspIleLeuLeuThrGlnSerProAlaIleLeuSerValSerProGlyGluArgValSer

TTCTCCTGCAGGGCCAGTCAGTTCGTTGGCTCAAGCATCCACTGGTATCAGCAAAGAACA
PheSerCysArgAlaSerGlnPheValGlySerSerIleHisTrpTyrGlnGlnArgThr

AATGGTTCTCCAAGGCTTCTCATAAAGTATGCTTCTGAGTCTATGTCTGGGATCCCTTCC
AsnGlySerProArgLeuLeuIleLysTyrAlaSerGluSerMetSerGlyIleProSer

AGGTTTAGTGGCAGTGGATCAGGGACAGATTTTACTCTTAGCATCAACACTGTGGAGTCT
ArgPheSerGlySerGlySerGlyThrAspPheThrLeuSerIleAsnThrValGluSer

GAAGATATTGCAGATTATTACTGTCAAGAAAGTCATAGCTGGCCATTCACGTTCGGCTCG
GluAspIleAlaAspTyrTyrCysGlnGlnSerHisSerTrpProPheThrPheGlySer

GGGACAAATTTGGAAGTAAAA
GlyThrAsnLeuGluValLys

FIG. 16A

862780"6TTEET60

GAAGTGAAGCTTGAGGAGTCTGGAGGAGGCTTGGTGCAACCTGGAGGATCCATGAAACTC
GluValLysLeuGluGluSerGlyGlyGlyLeuValGlnProGlyGlySerMetLysLeu

TCCTGTGTTGCCTCTGGATTCATTTTCAGTAACCACTGGATGAACTGGGTCCGCCAGTCT
SerCysValAlaSerGlyPheIlePheSerAsnHisTrpMetAsnTrpValArgGlnSer

CCAGAGAAGGGGCTTGAGTGGGTTGCTGAAATTAGATCAAAATCTATTAATTCTGCAACA
ProGluLysGlyLeuGluTrpValAlaGluIleArgSerLysSerIleAsnSerAlaThr

CATTATGCGGAGTCTGTGAAAGGGAGGTTCACCATCTCAAGAGATGATTCCAAAAGTGCT
HisTyrAlaGluSerValLysGlyArgPheThrIleSerArgAspAspSerLysSerAla

GTGTACCTGCAAATGACCGACTTAAGAACTGAAGACACTGGCGTTTATTACTGTTCCAGG
ValTyrLeuGlnMetThrAspLeuArgThrGluAspThrGlyValTyrTyrCysSerArg

AATTACTACGGTAGTACCTACGACTACTGGGGCCAAGGCACCACTCTCACAGTGTCC
AsnTyrTyrGlySerThrTyrAspTyrTrpGlyGlnGlyThrThrLeuThrValSer

FIG. 16B

862780 6TEET60

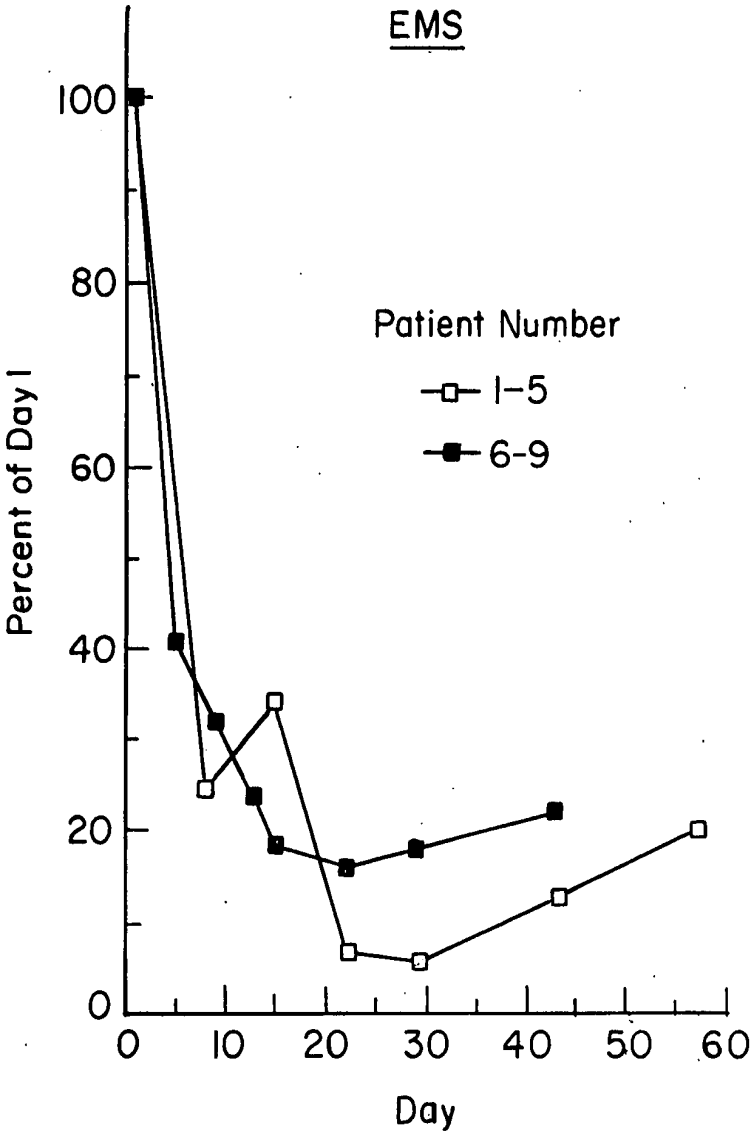


FIG. 17

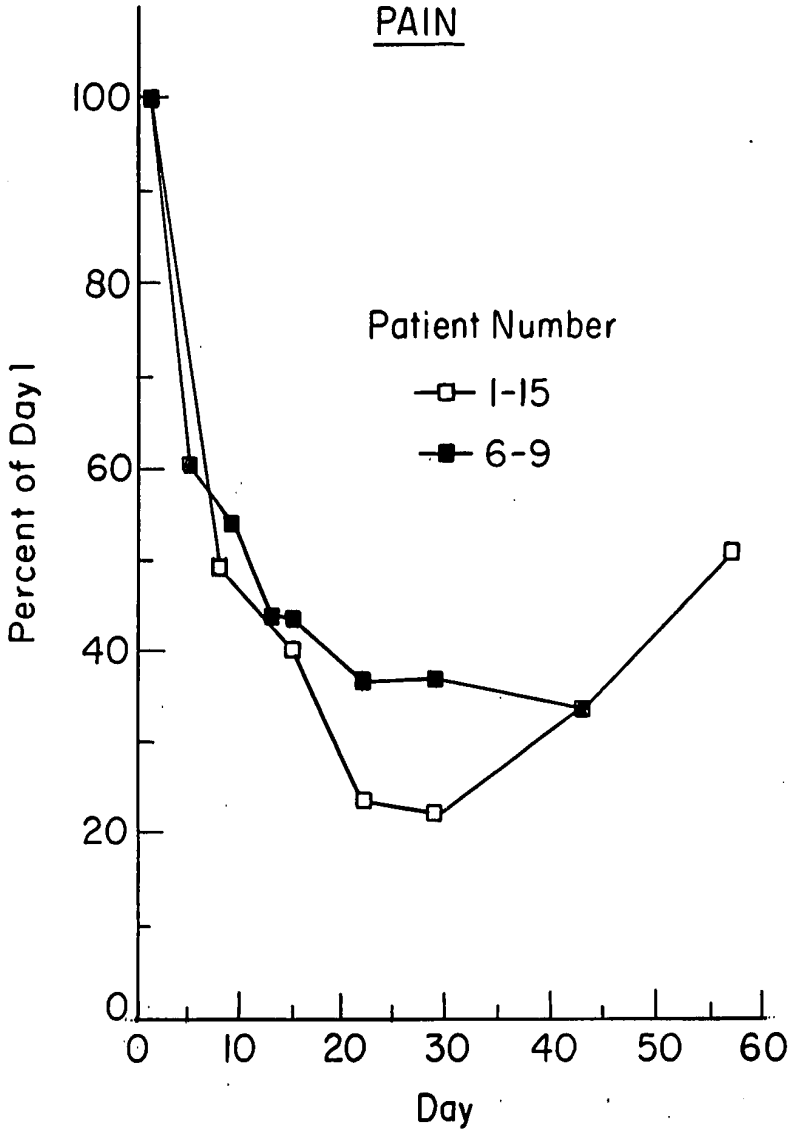


FIG. 18

862780 "6TTEET60

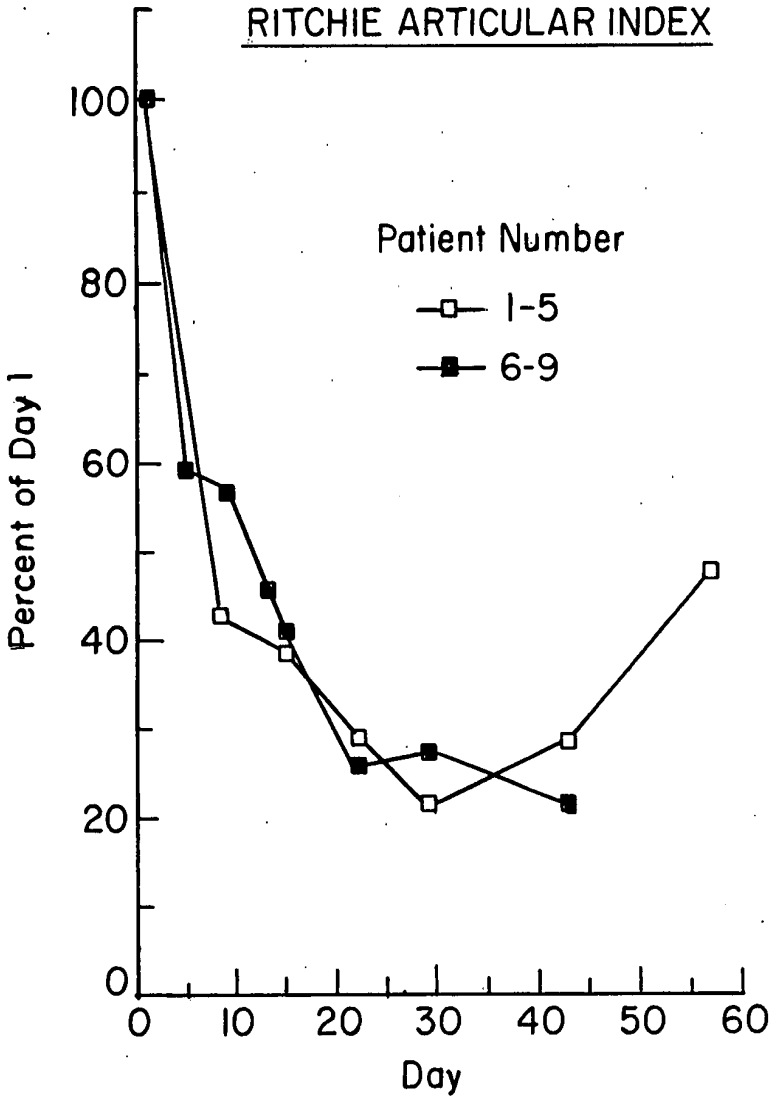


FIG. 19

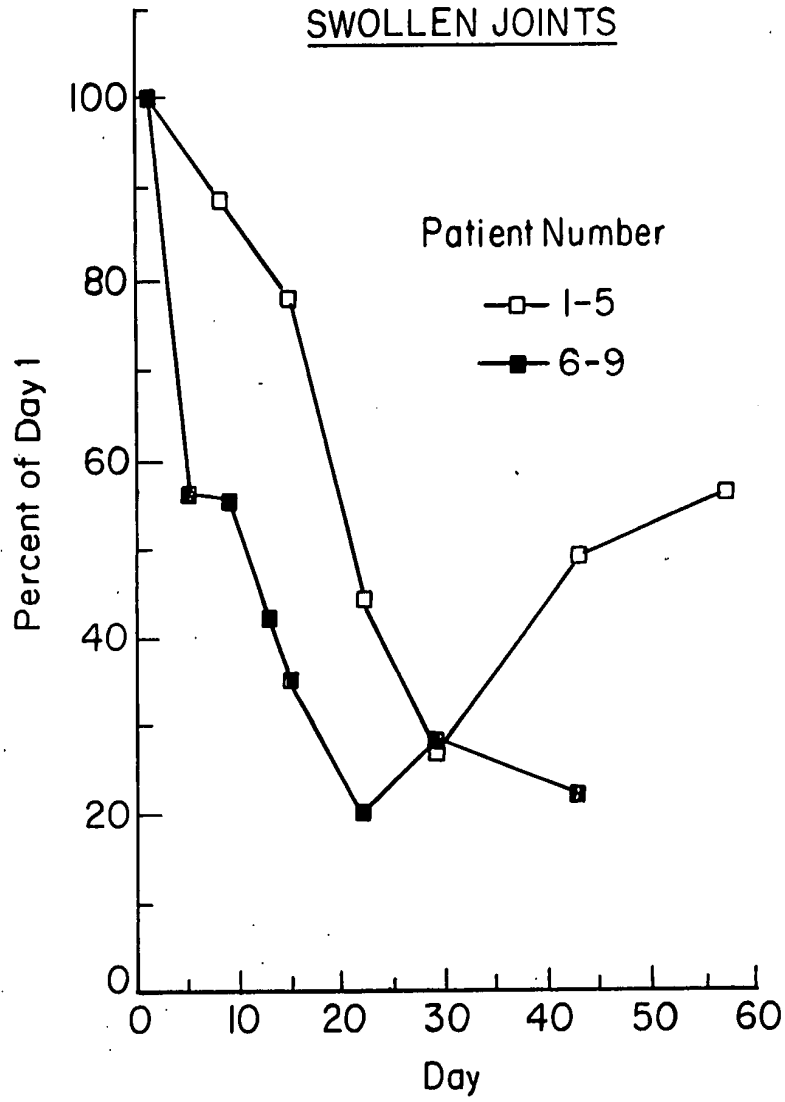


FIG. 20

862780 6TTEET60

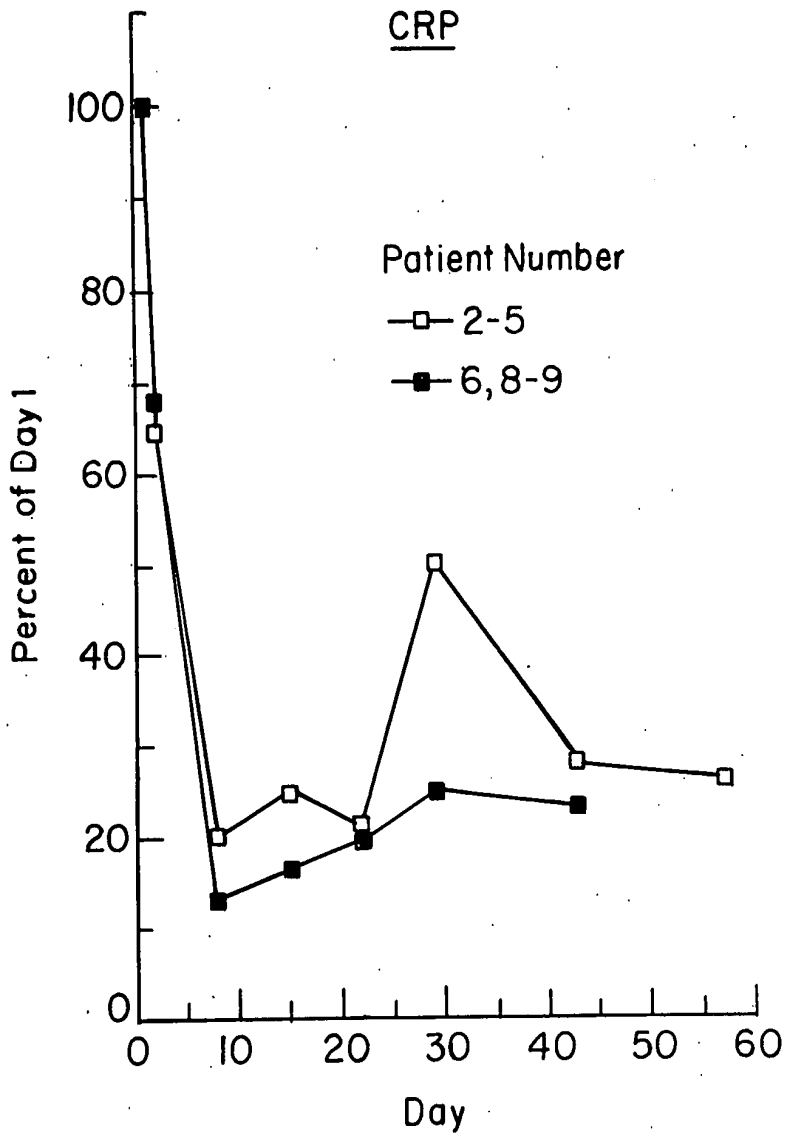


FIG. 21

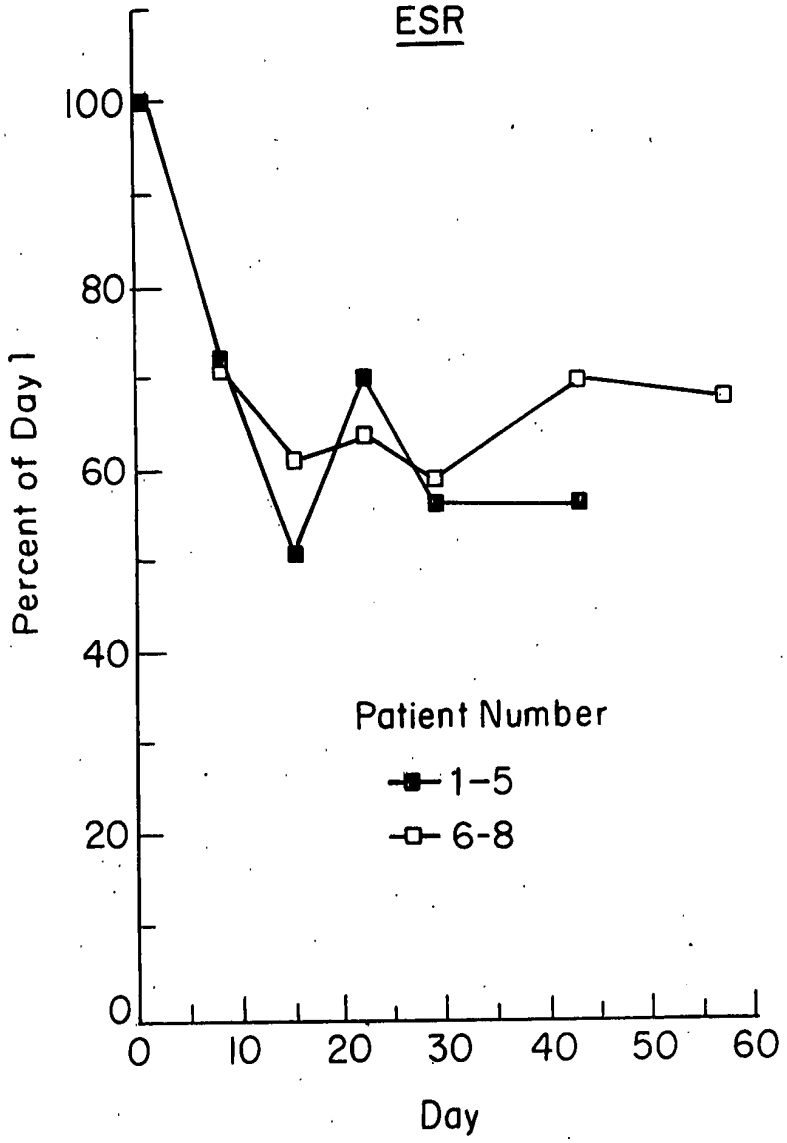


FIG. 22

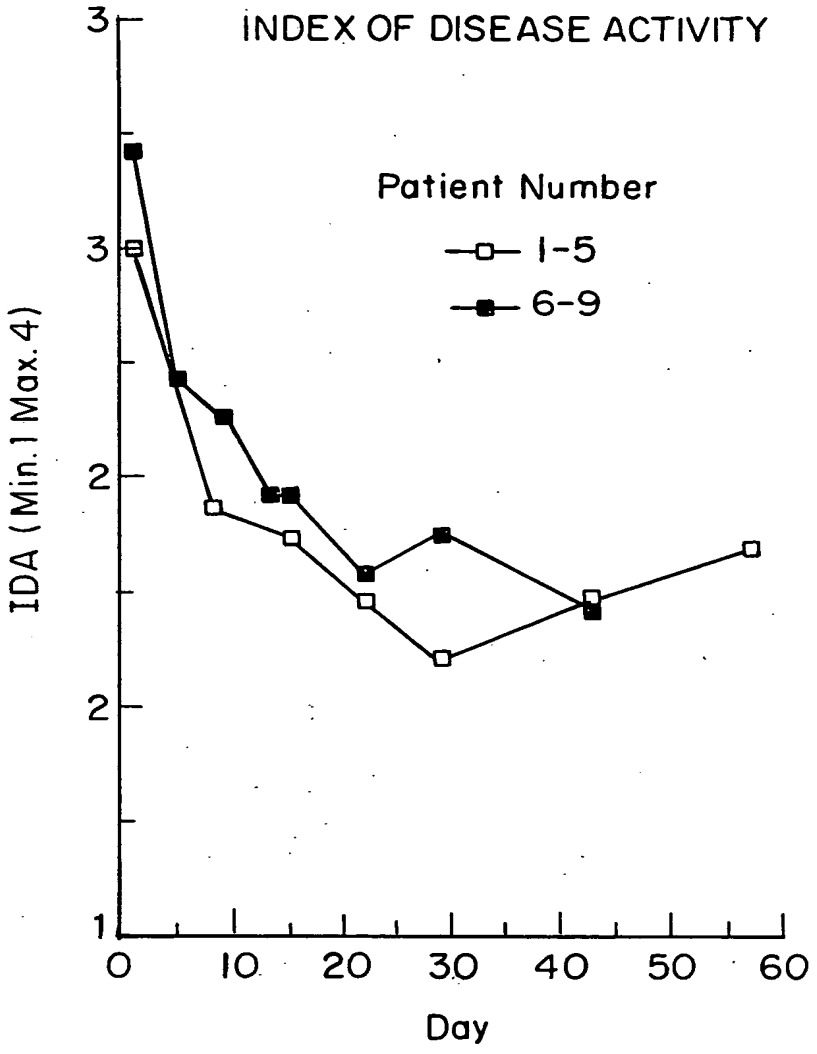

INDEX OF DISEASE ACTIVITY
Patient Number
1-5
6-9
IDA (Min. 1 Max. 4)
3
3
2
2
1
0
10
20
30
40
50
60
Day

FIG. 23

862780 6TTEET60

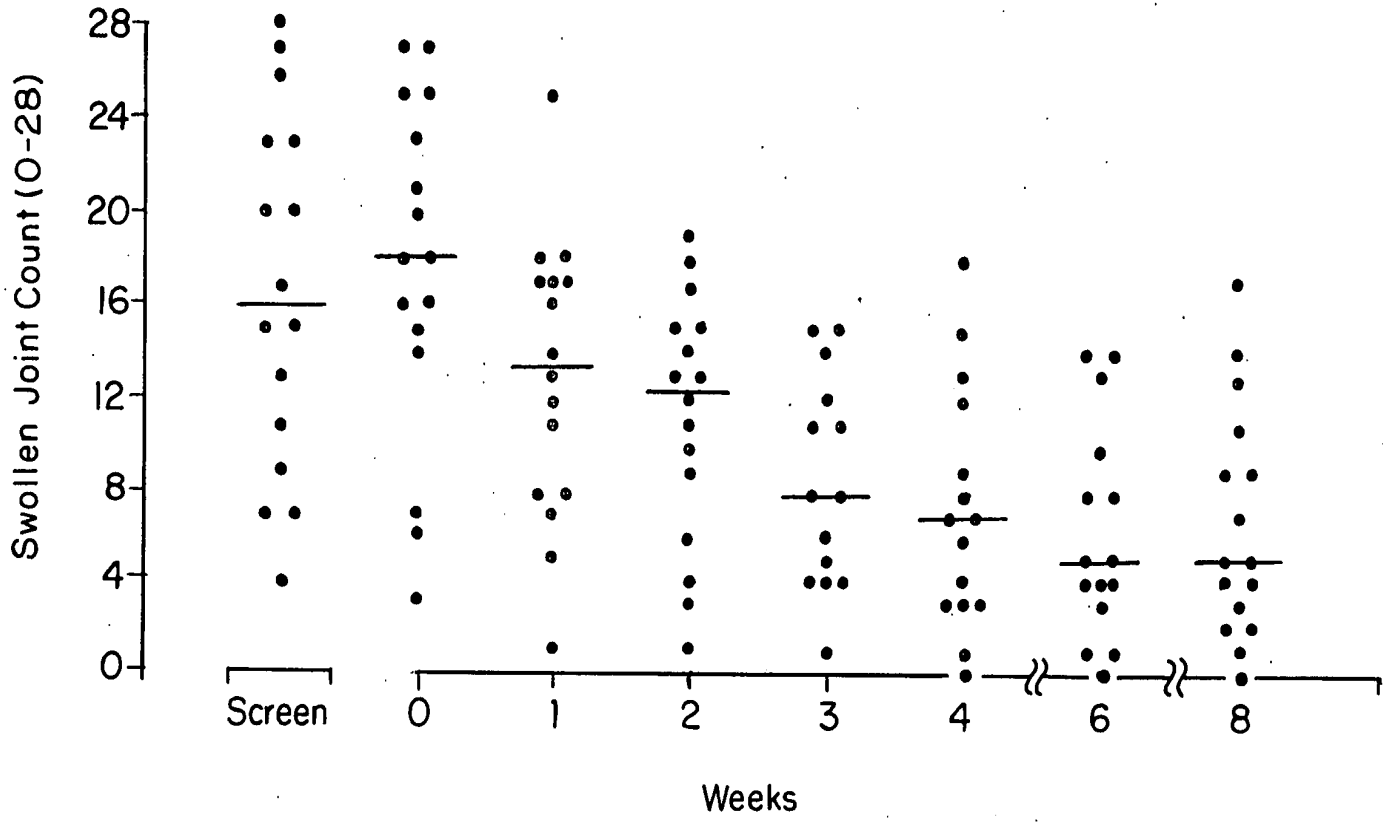


FIG. 24

862T80"6TTEET60

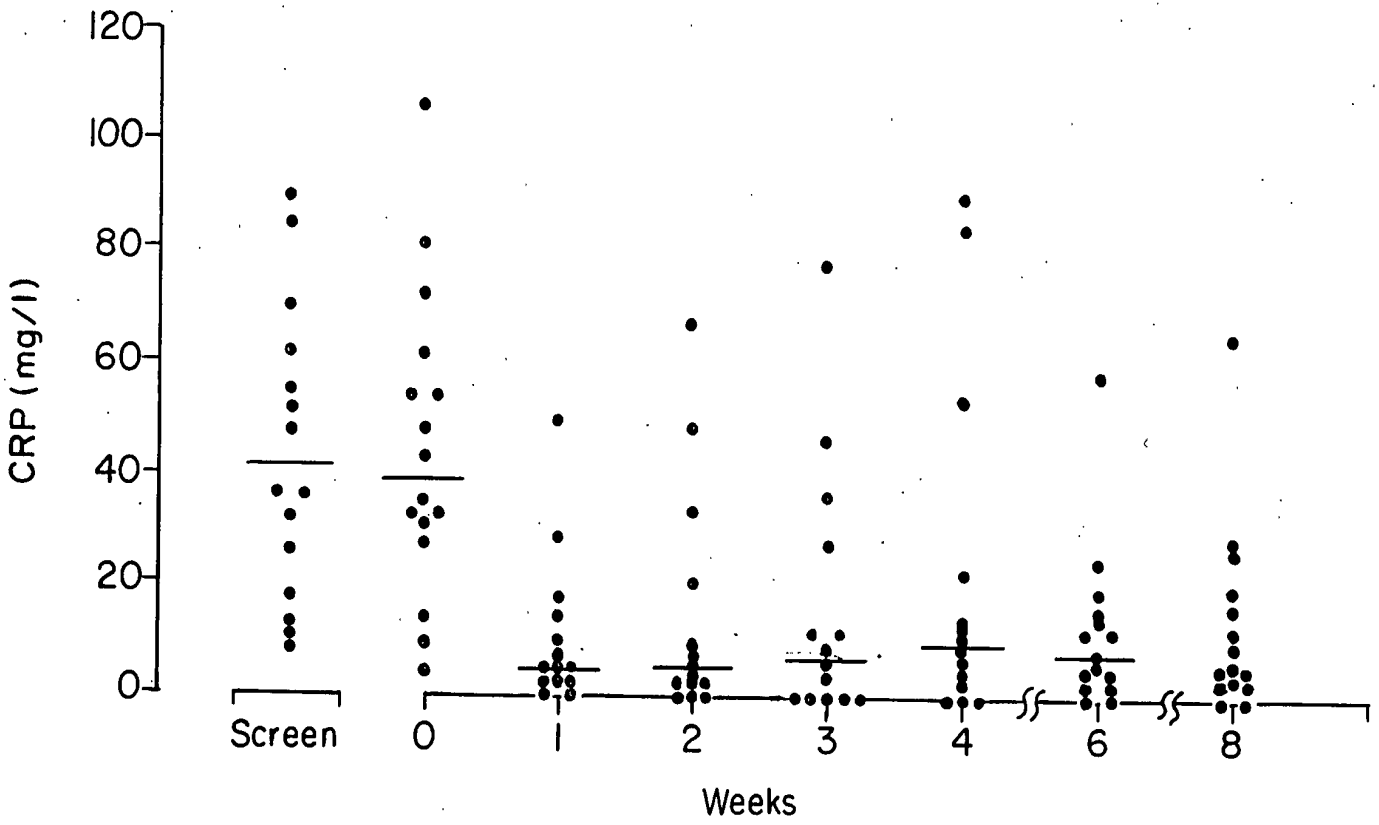


FIG. 25

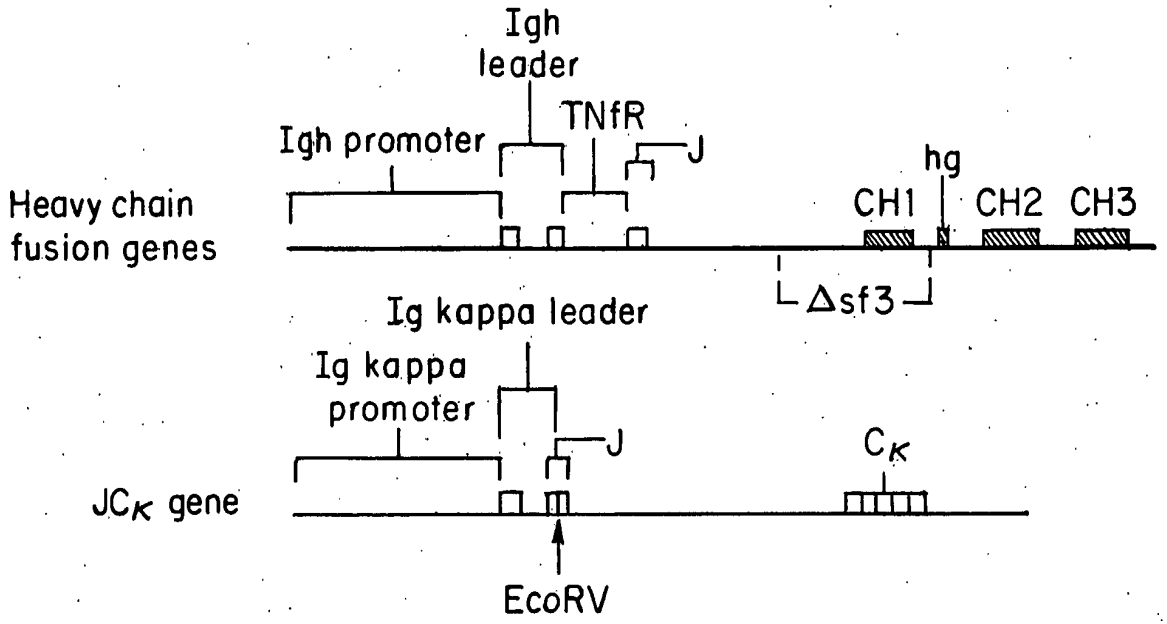

Igh
leader
TNfR
Igh promoter
J
hg
Heavy chain
fusion genes
CH1
CH2
CH3
Δsf3
Ig kappa leader
Ig kappa
promoter
J
C_K
JC_K gene
EcoRV

FIG. 26A

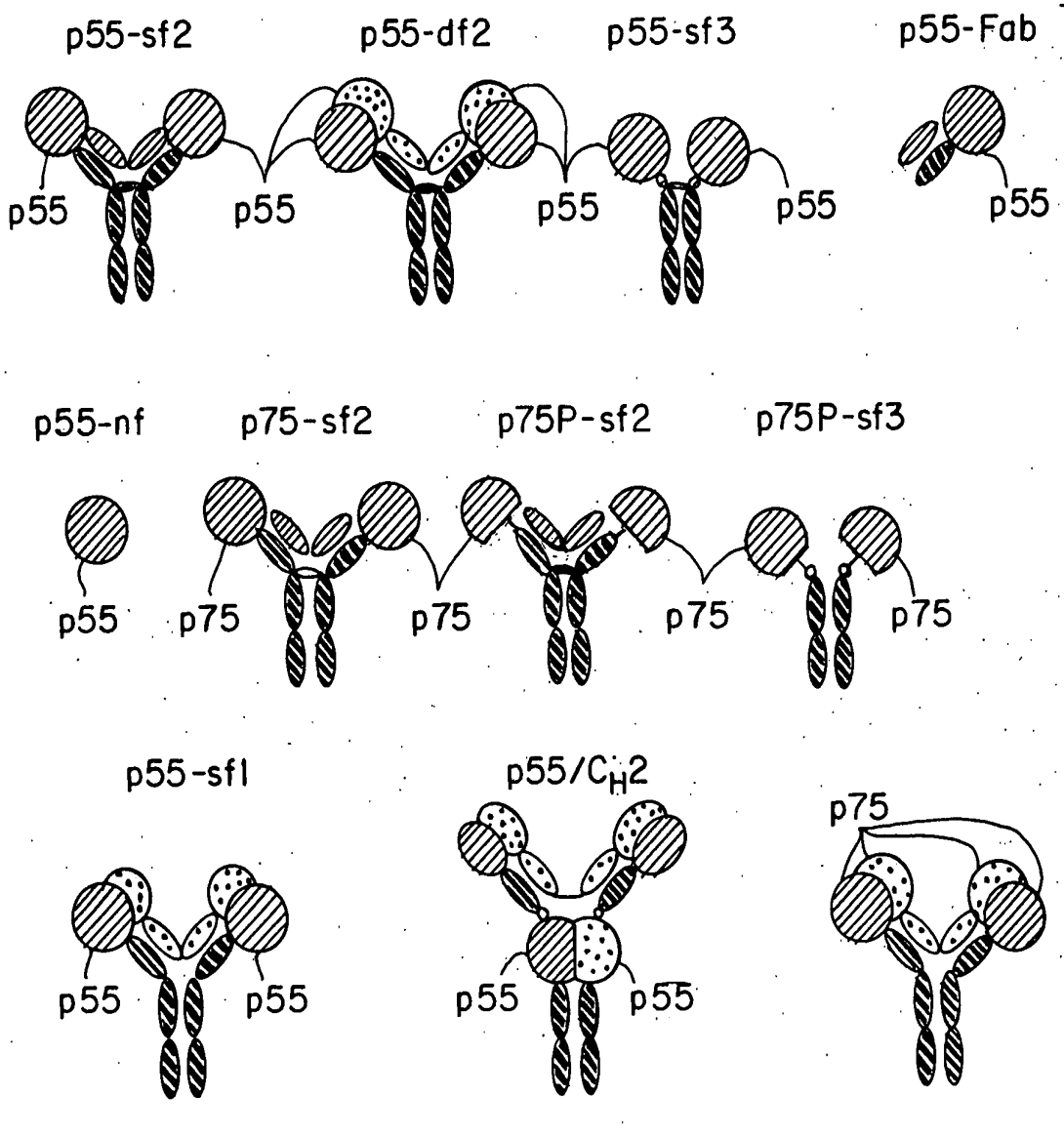

p55-sf2
p55-df2
p55-sf3
p55-Fab
p55
p55
p55
p55
p55
p55-nf
p75-sf2
p75P-sf2
p75P-sf3
p55
p75
p75
p75
p75
p55-sf1
p55/C_H2
p75
p55
p55
p55
p55

FIG. 26B

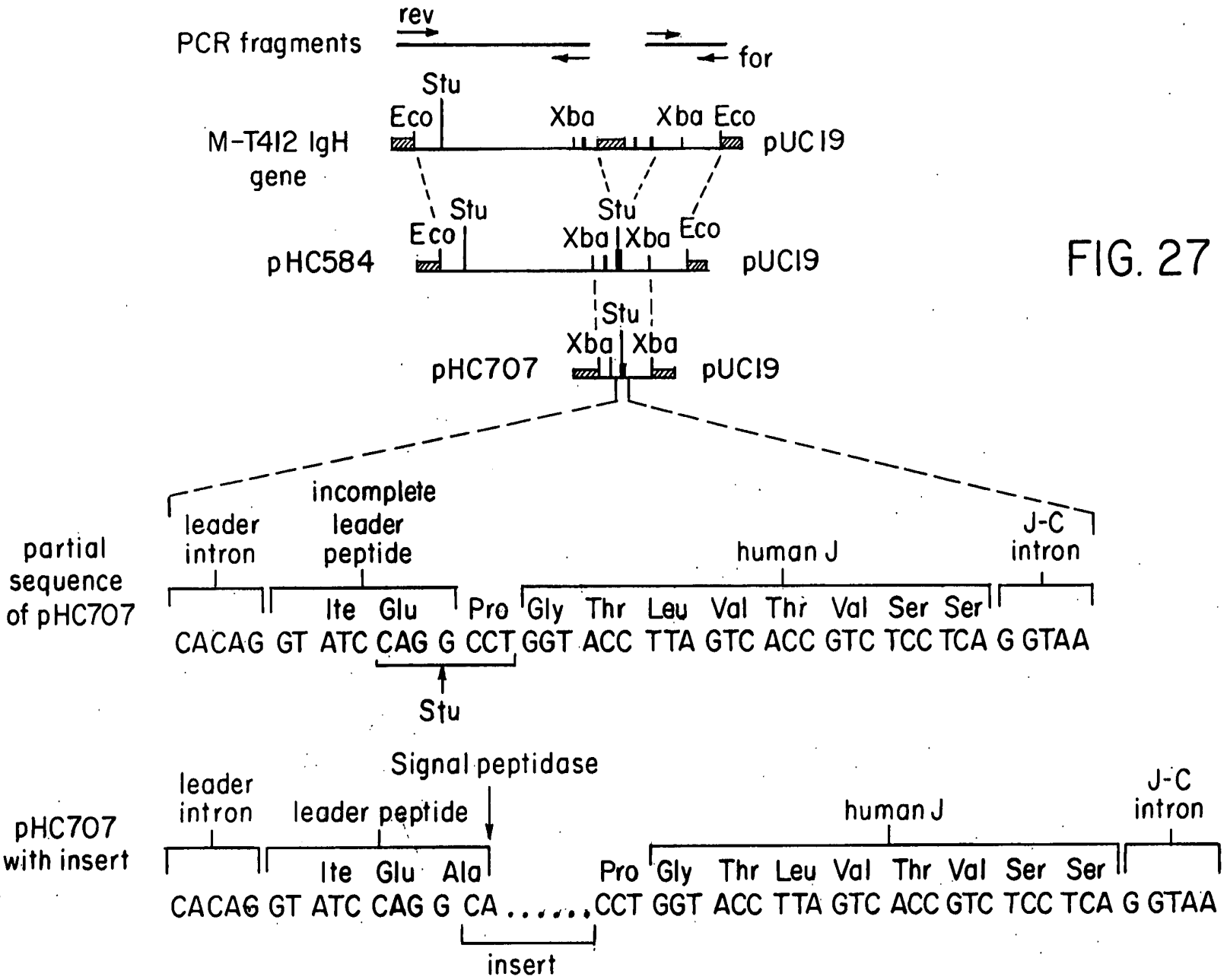

PCR fragments
rev
for
M-T412 IgH gene
Stu
Eco
Xba
Xba Eco
pUC19
pHC584
Stu
Eco
Stu
Xba Xba
Eco
pUC19
pHC707
Stu
Xba Xba
pUC19
partial sequence of pHC707
leader intron
incomplete leader peptide
human J
J-C intron
Ile Glu Pro Gly Thr Leu Val Thr Val Ser Ser
CACAG GT ATC CAG G CCT GGT ACC TTA GTC ACC GTC TCC TCA G GTAA
Stu
pHC707 with insert
leader intron
Signal peptidase
leader peptide
human J
J-C intron
Ile Glu Ala Pro Gly Thr Leu Val Thr Val Ser Ser
CACAG GT ATC CAG G CA ..... CCT GGT ACC TTA GTC ACC GTC TCC TCA G GTAA
insert

FIG. 27

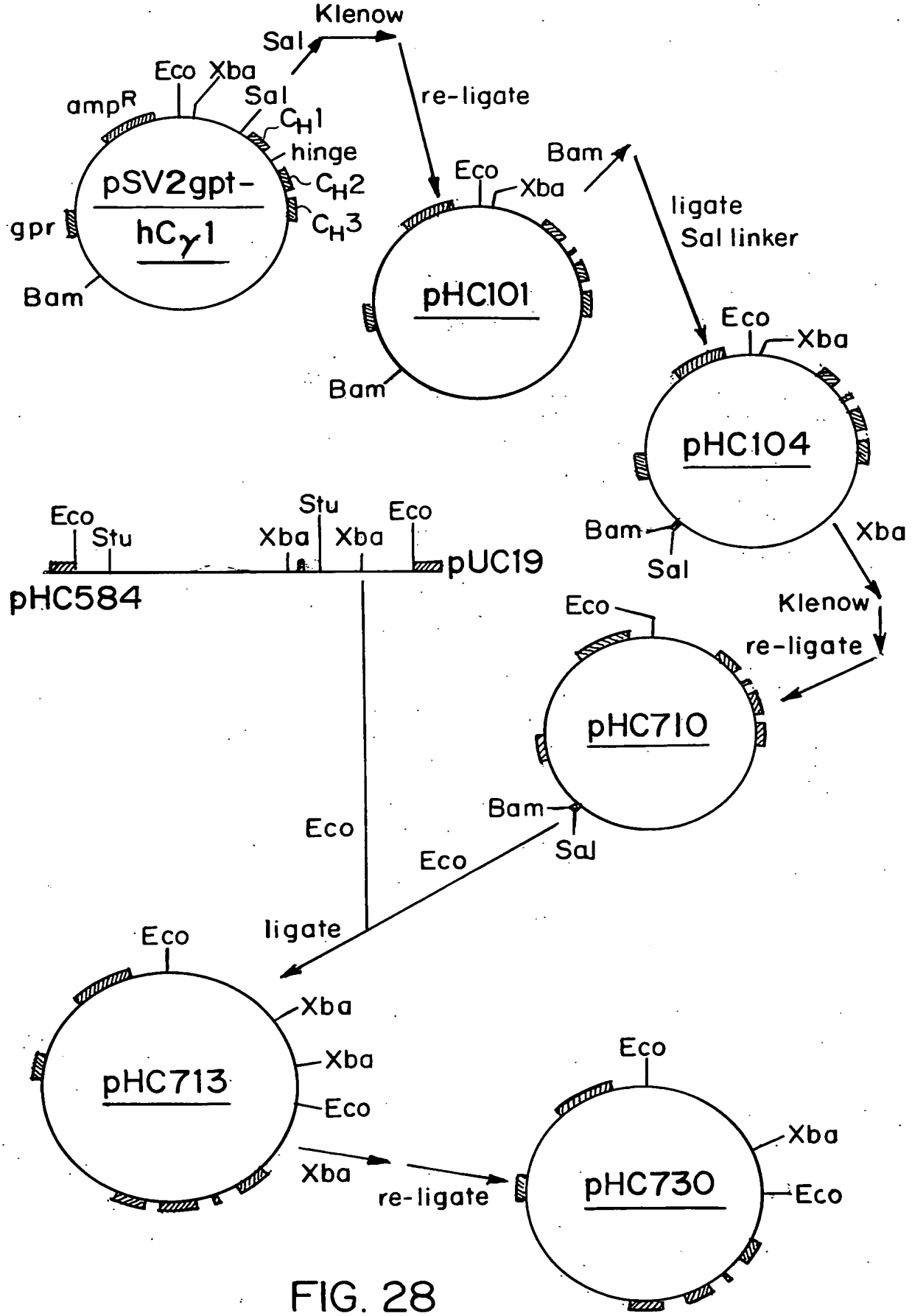

Klenow
Sal
Eco Xba
Sal
ampR
C_H1
hinge
C_H2
C_H3
pSV2gpt-
hCγ1
gpr
Bam
re-ligate
Eco
Xba
pHC101
Bam
Bam
ligate
Sal linker
Eco
Xba
pHC104
Bam
Sal
Xba
Eco
Stu
Stu
Xba
Xba
Eco
pUC19
pHC584
Klenow
re-ligate
Eco
pHC710
Bam
Sal
Eco
Eco
ligate
Eco
Xba
Xba
pHC713
Eco
Xba
re-ligate
Eco
Xba
pHC730
Eco

FIG. 28

862180 6TTEET60

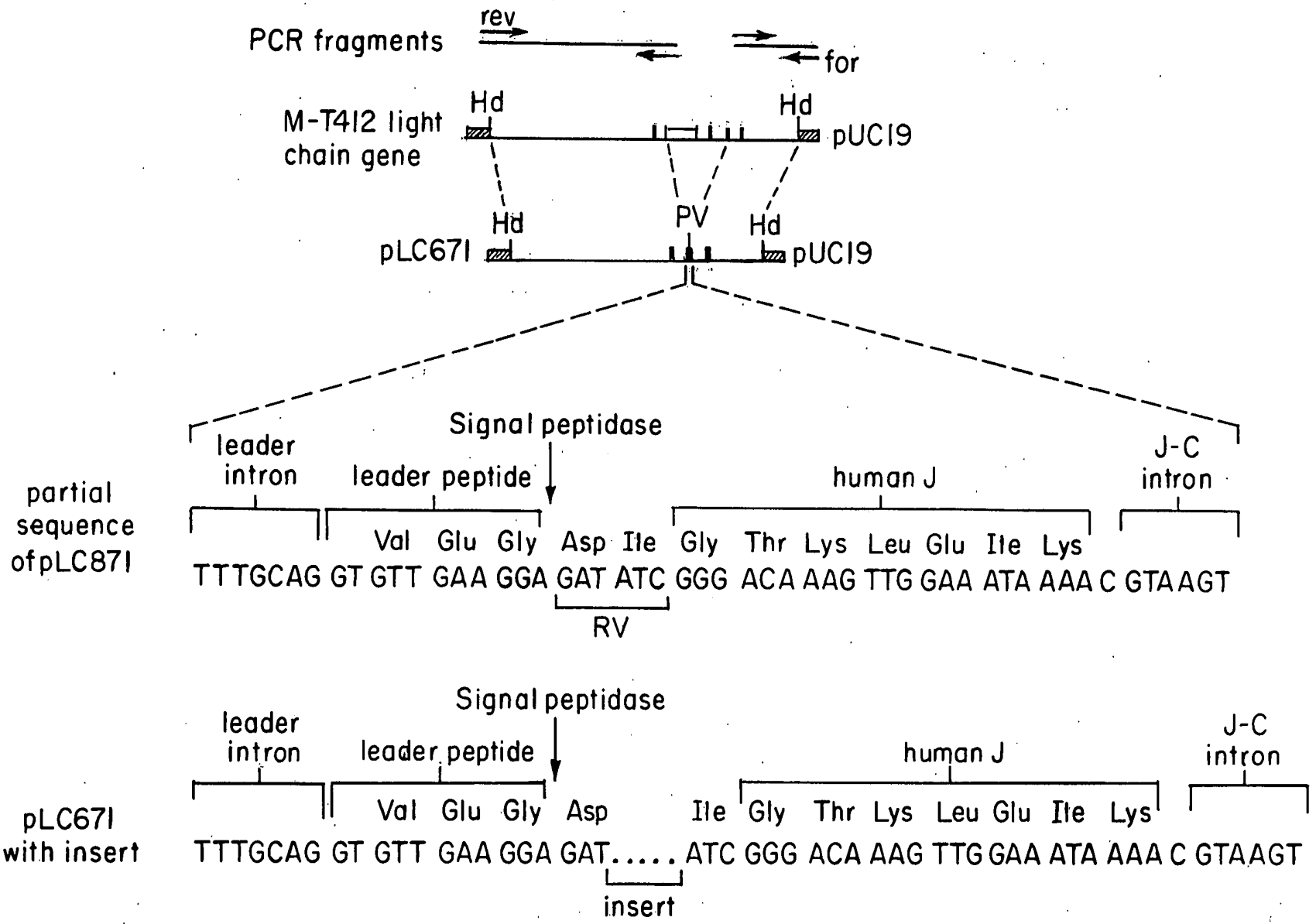


FIG. 29

86278-6714-0834

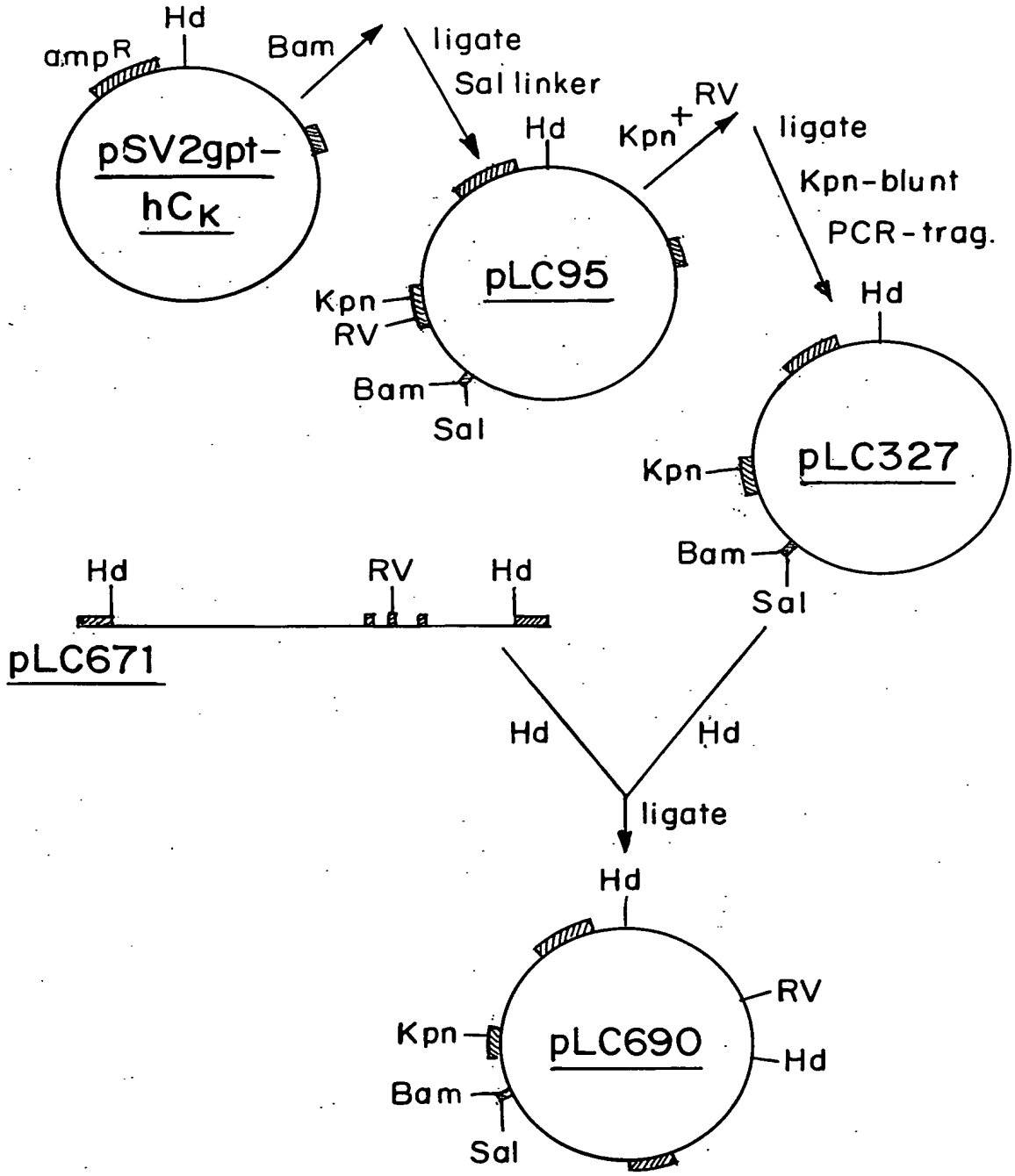


FIG. 30

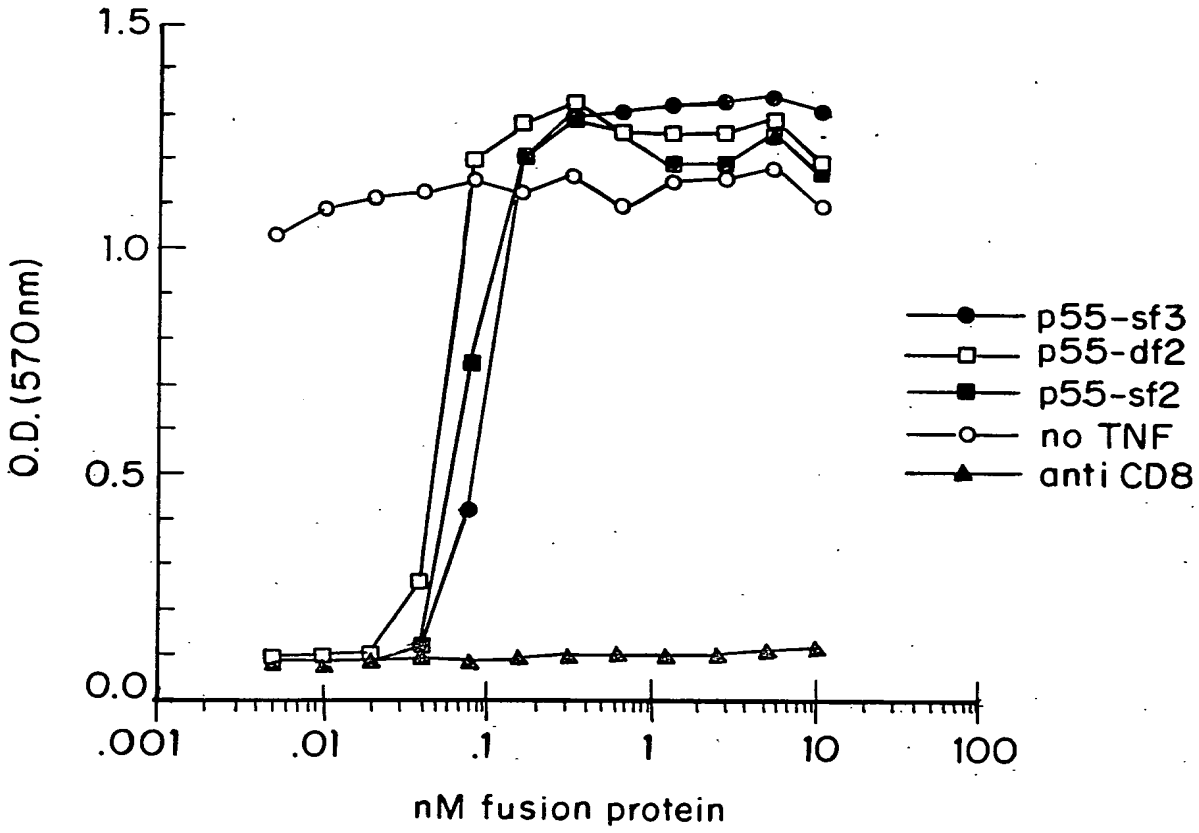

1.5
1.0
0.5
0.0
O.D.(570nm)
.001
.01
.1
1
10
100
nM fusion protein
p55-sf3
p55-df2
p55-sf2
no TNF
anti CD8

FIG. 31A

95280-5TE60

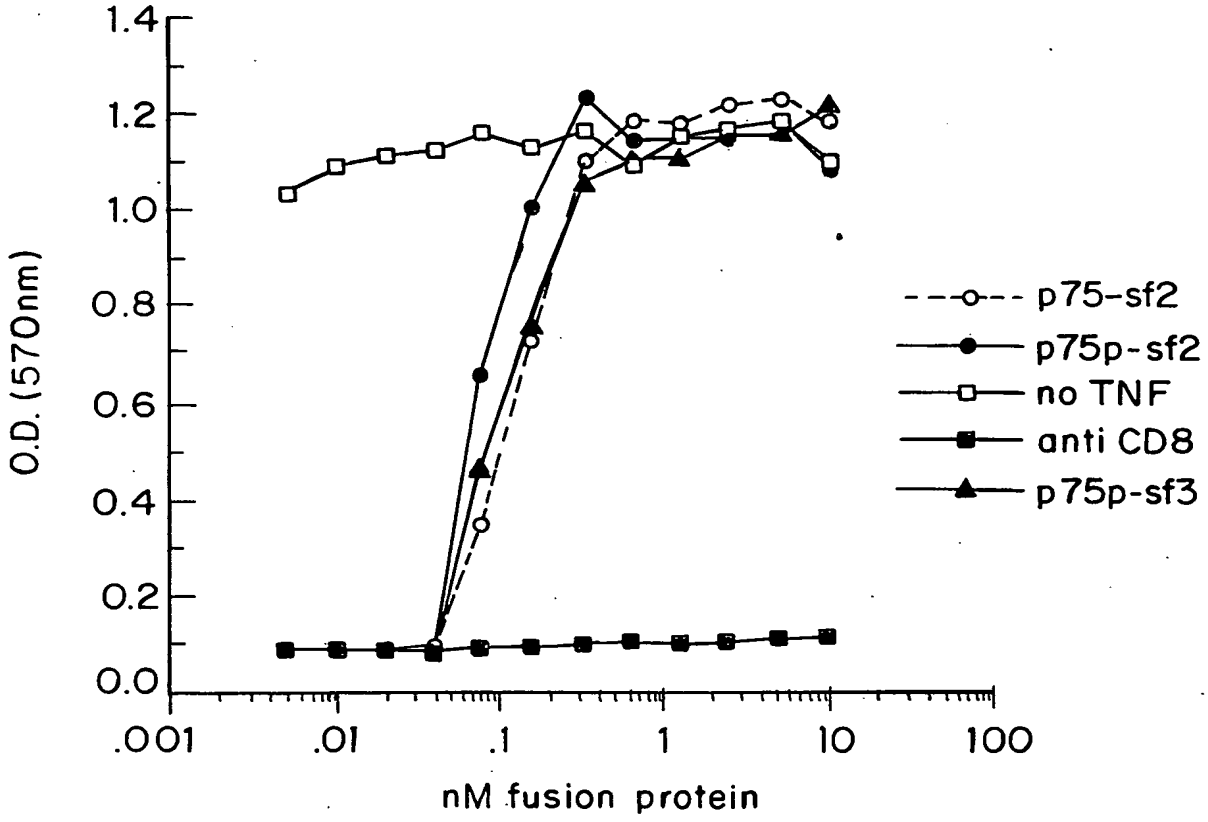


FIG. 31B

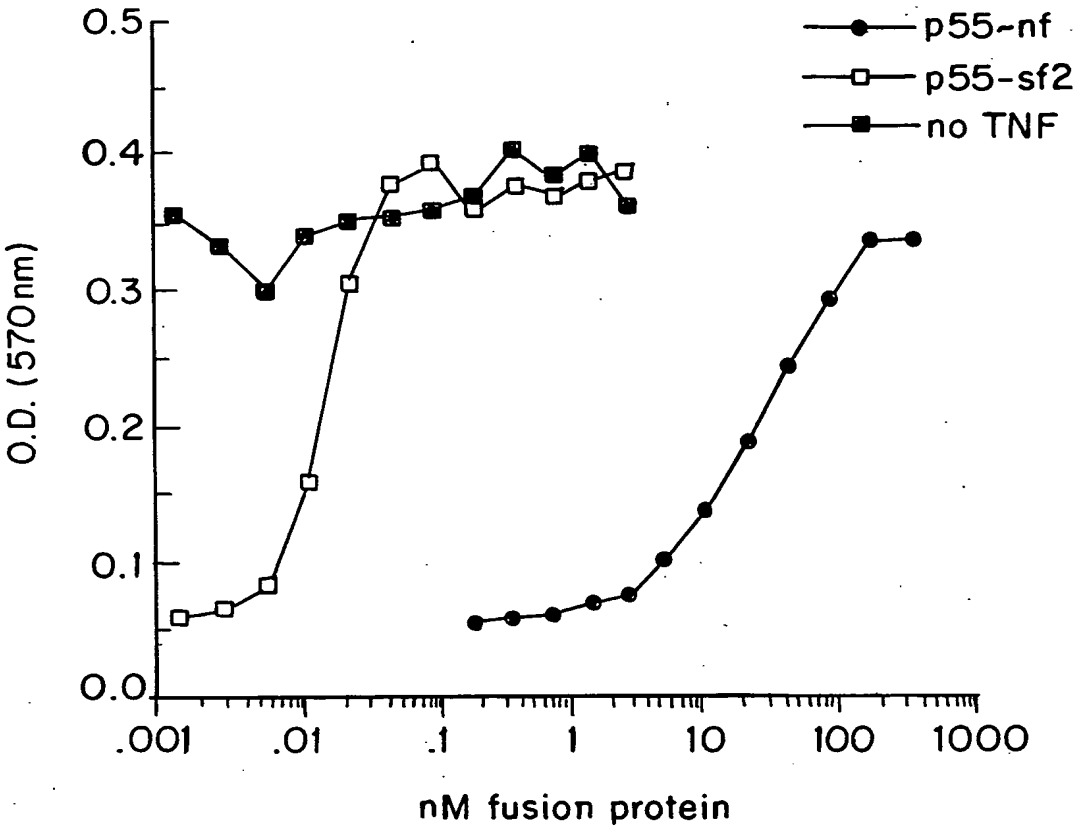


FIG. 31C

0234-0234-0234-0234

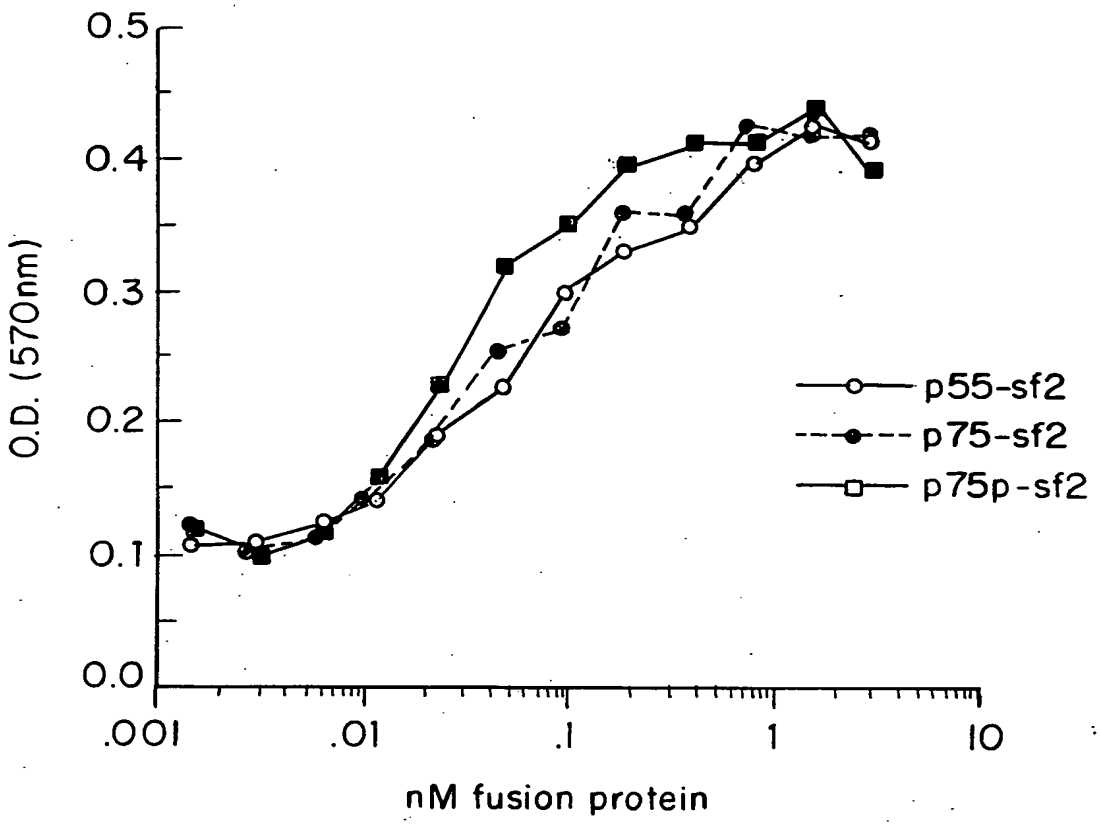

0.5
0.4
0.3
0.2
0.1
0.0
O.D. (570nm)
.001
.01
.1
1
10
nM fusion protein
p55-sf2
p75-sf2
p75p-sf2

FIG. 32

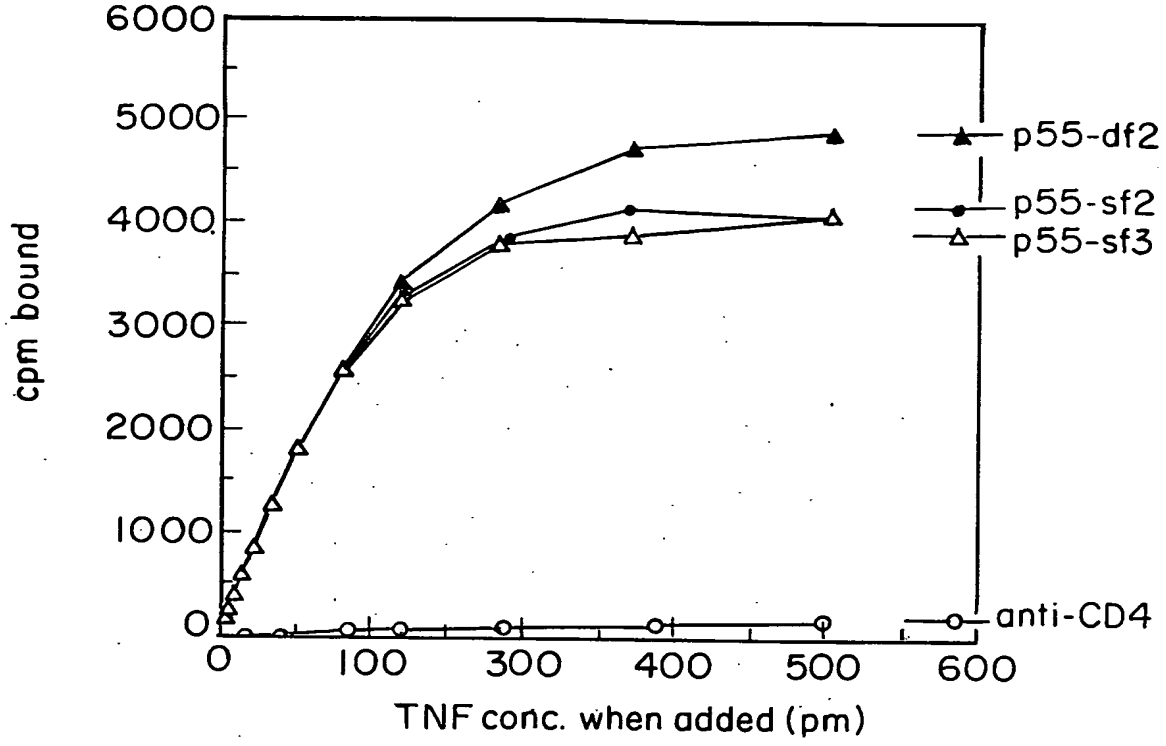


FIG. 33A

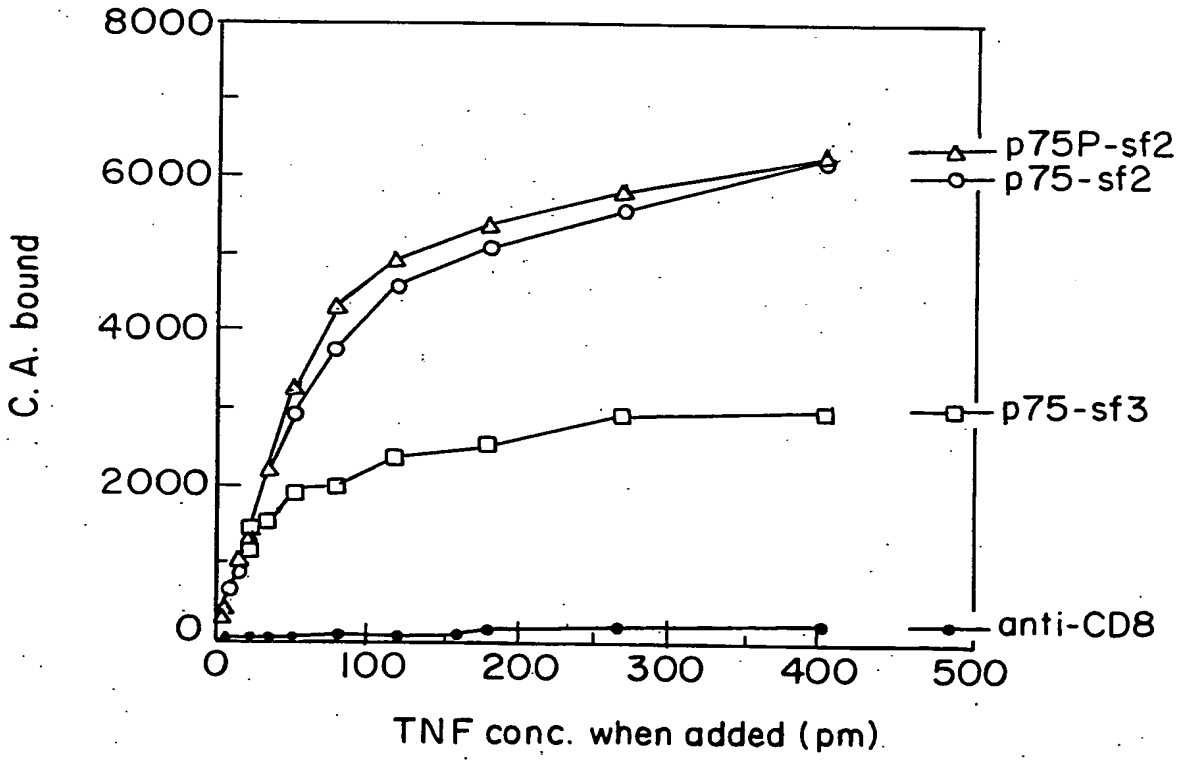


FIG. 33B

08/480,676

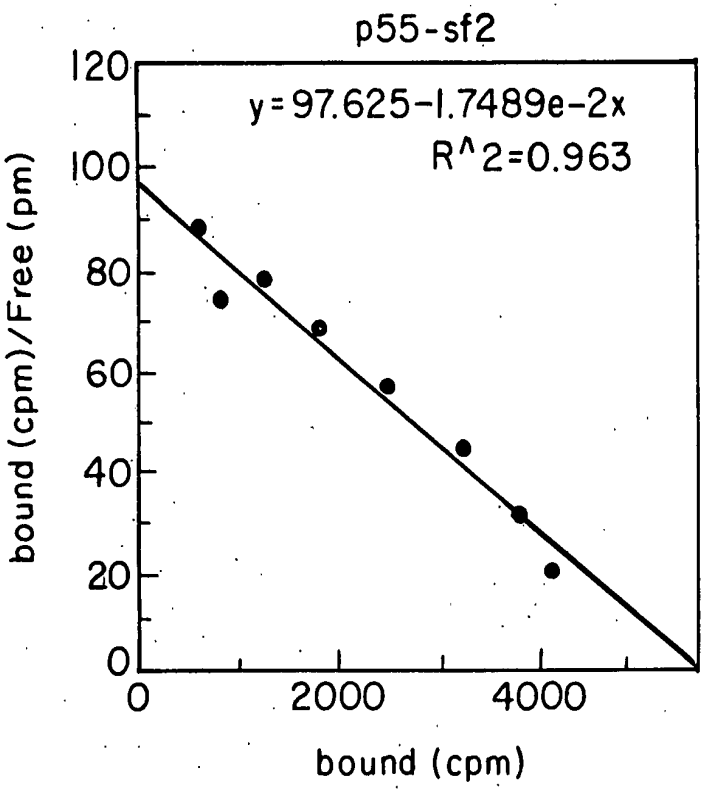


FIG. 33C

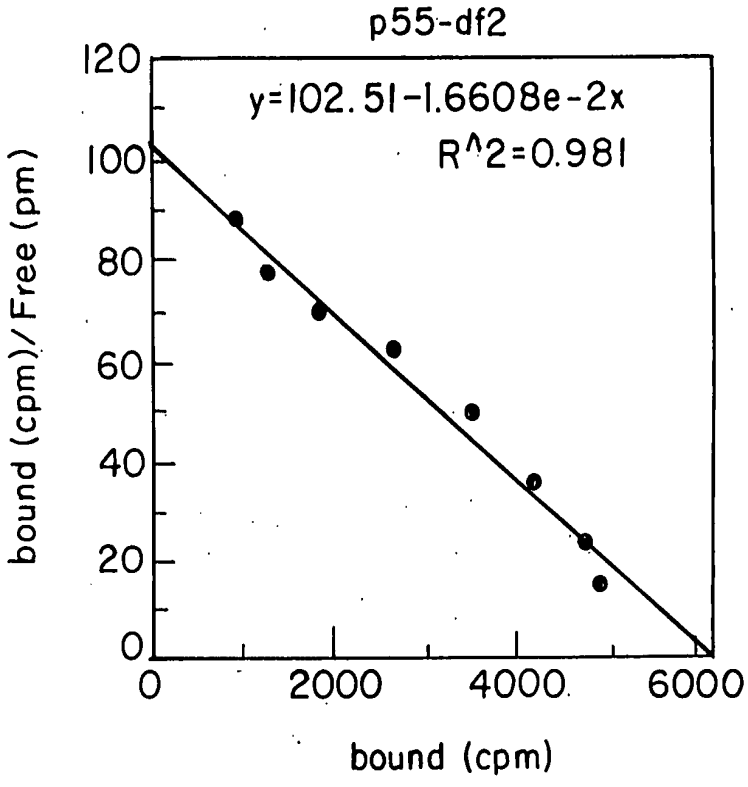


FIG. 33D

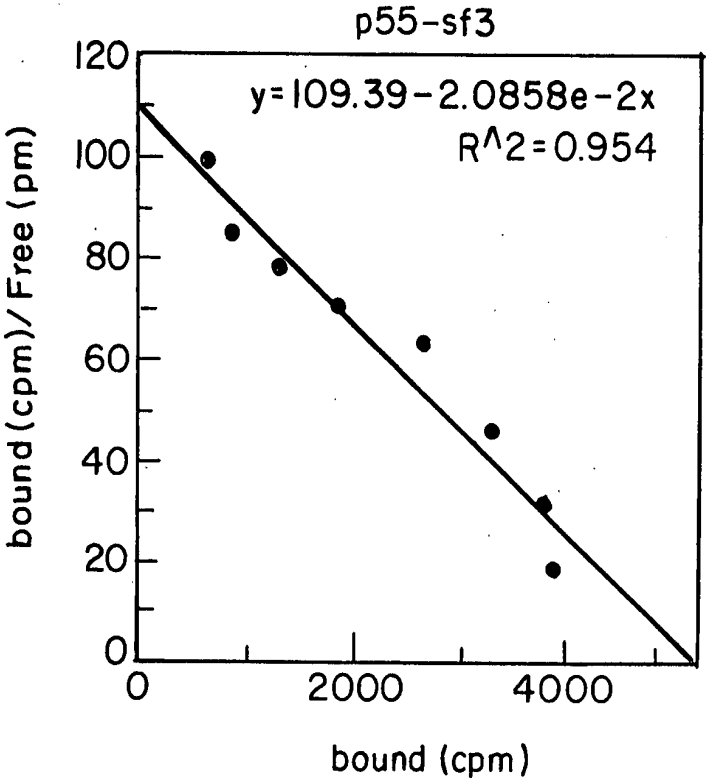


FIG. 33E

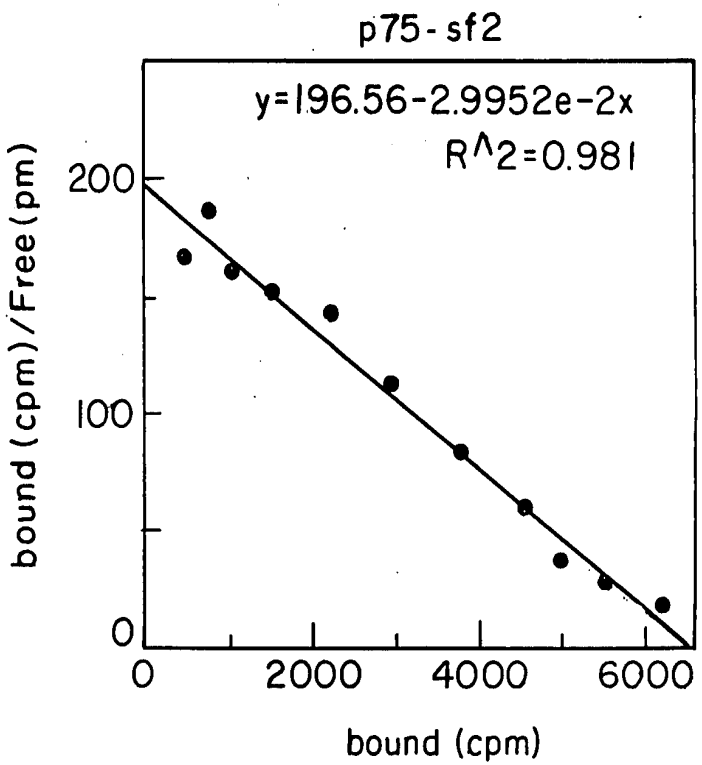


FIG. 33F

862180 6TTEE160

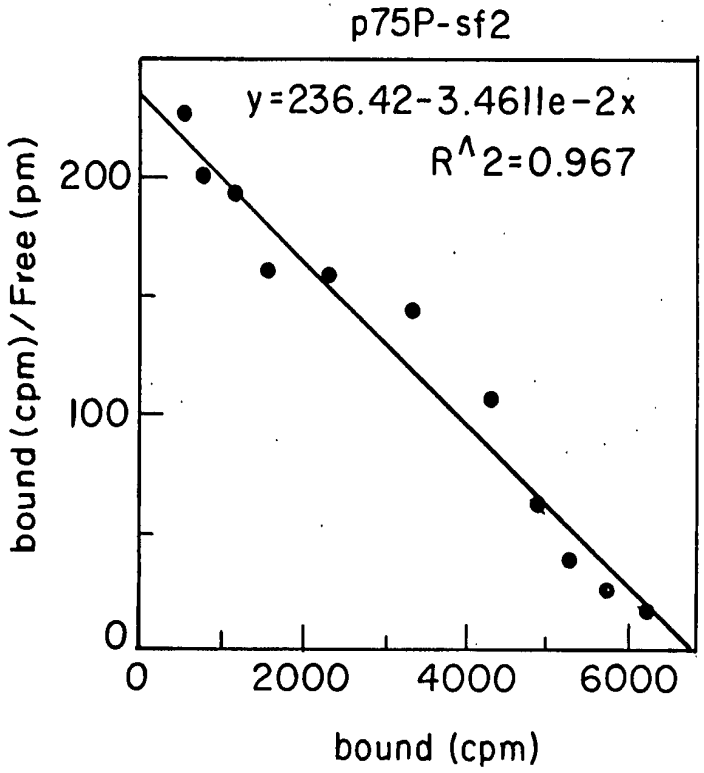


FIG. 33G

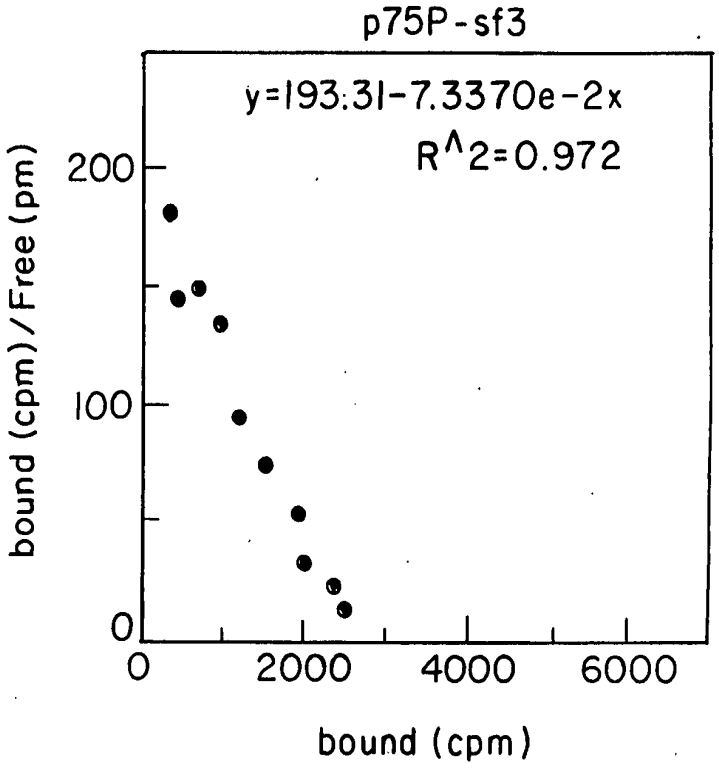
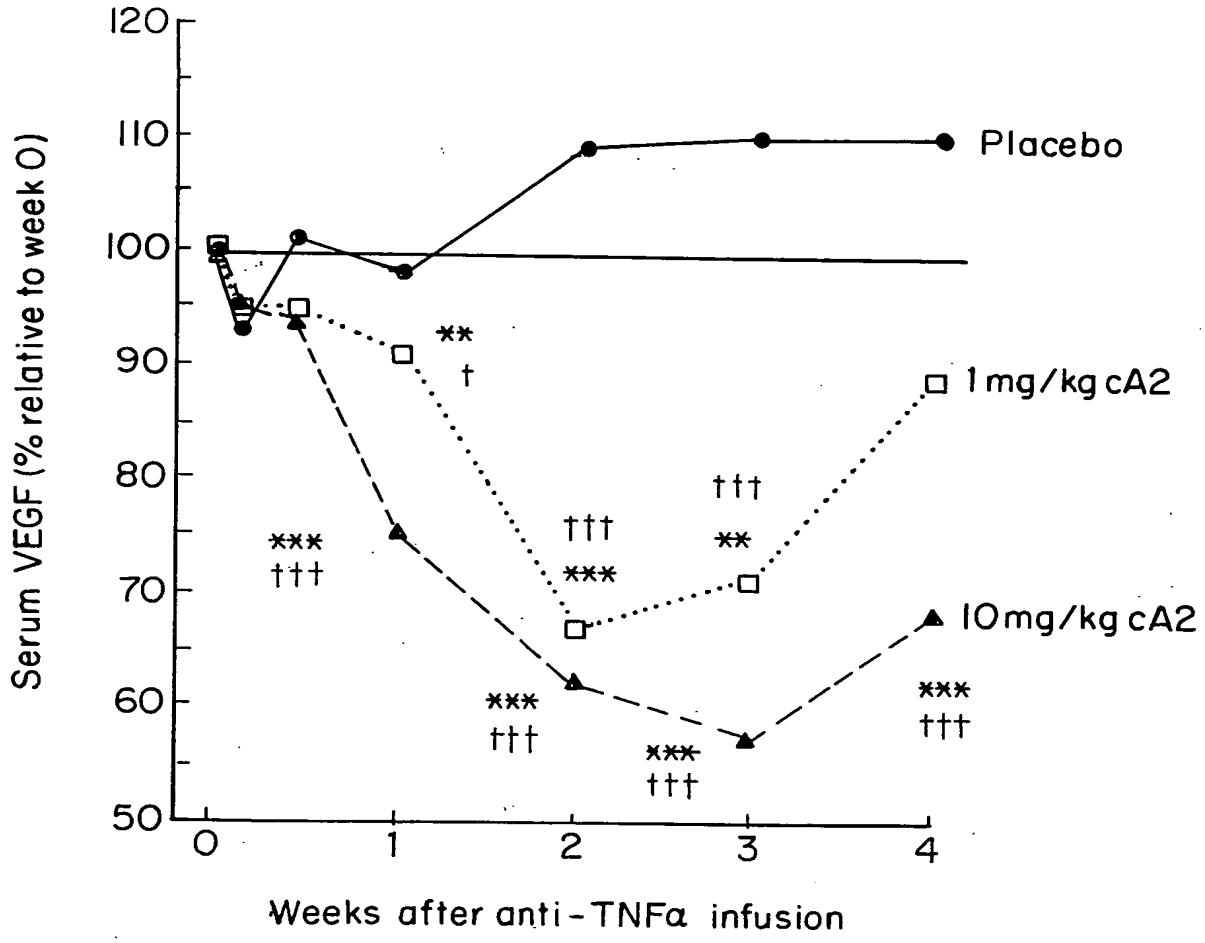


FIG. 33H



* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$ *versus* pre-infusion
† $p \leq 0.05$, †† $p \leq 0.01$, ††† $p \leq 0.001$ *versus* change in placebo group

FIG. 34